(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) **EP 3 328 860 B2**

(12) **NEW EUROPEAN PATENT SPECIFICATION**
After opposition procedure

(45) Date of publication and mention of the opposition decision:
02.11.2022 Bulletin 2022/44

(45) Mention of the grant of the patent:
04.03.2020 Bulletin 2020/10

(21) Application number: **16745684.7**

(22) Date of filing: **26.07.2016**

(51) International Patent Classification (IPC):
C07D 487/04 *(2006.01)*

(52) Cooperative Patent Classification (CPC):
C07D 487/04

(86) International application number:
PCT/EP2016/067789

(87) International publication number:
WO 2017/017096 (02.02.2017 Gazette 2017/05)

(54) **PROCESS FOR THE PREPARATION OF BENZIMIDAZO[1,2-A]BENZIMIDAZOLES**

PROZESS ZUR HERSTELLUNG VON BENZIMIDAZO[1,2-A]BENZIMIDAZOLEN

PROCÉDÉ POUR LA PRÉPARATION DE BENZIMIDAZO[1,2-A]BENZIMIDAZOLES

(84) Designated Contracting States:
AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO PL PT RO RS SE SI SK SM TR

(30) Priority: **28.07.2015 EP 15178573**

(43) Date of publication of application:
06.06.2018 Bulletin 2018/23

(73) Proprietor: **UDC Ireland Limited**
Ballycoolin, Dublin 15 (IE)

(72) Inventors:
- **GREEF, DE, Michiel**
  Dublin 15 (IE)
- **PETER, Bernd**
  Dublin 15 (IE)
- **STUMPF, Ruediger**
  Dublin 15 (IE)

(74) Representative: **Maiwald Patent- und Rechtsanwaltsgesellschaft mbH**
Elisenhof
Elisenstraße 3
80335 München (DE)

(56) References cited:
WO-A1-2012/130709

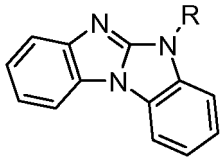
- **I.V. KOLESNIKOVA ET AL: "Reactions of N-polyfluorophenylcarbonimidoyl dichlorides with primary and secondary amines. Kinetics and mechanism. Synthesis of polyfluorinated carbodiimides, chloroformamidines, guamidines and benzimidazoles.", JOURNAL OF FLUORINE CHEMISTRY, vol. 40, no. 2-3, 1 August 1988 (1988-08-01), pages 217-246, XP055213650, ISSN: 0022-1139, DOI: 10.1016/S0022-1139(00)83067-5**
- **REDDOUANE ACHOUR ET AL: "Syntheses des Benzimidazolo (1,2-a) Benzimidazoles A Partir des Benzodiazepine-1, 5Ones-2", BULLETIN DES SOCIÉTÉS CHIMIQUES BELGES : VLAAMSE CHEMISCHE VERENIGING, CENTERICK, BE, vol. 96, no. 10, 1 January 1987 (1987-01-01), pages 787-792, XP009123274, ISSN: 0037-9646 cited in the application**
- **Z. WU et al.: "Synthesis of Pyrido[1,2-a]benzimidazoles through a Copper-Catalyzed Cascade C-N Coupling Process", Eur. J. Org. Chem., vol. 2011, no. 27, 18 August 2011 (2011-08-18), pages 5242-5245,**
- **S. KUMAR et al.: "Efficient Routes to Pyrazolo[3,4- b]indoles and Pyrazolo[1,5- a]benzimidazoles via Palladium- and Copper-Catalyzed Intramolecular C?C and C?N Bond Formation", J. Org. Chem., vol. 74, no. 18, 18 September 2009 (2009-09-18), pages 7046-7051,**

EP 3 328 860 B2

Description

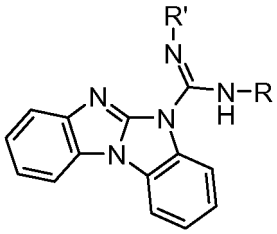
[0001] The present invention relates to process for the preparation of a compound of formula (I), which can be produced by the process easily, with excellent yield and purity and at low cost.

[0002] Khan, Misbahul Ain; Ribeiro, Vera Lucia Teixeira, Pakistan Journal of Scientific and Industrial Research 43 (2000) 168-170 describes the synthesis of benzimidazo[1,2-a]benzimadazoles

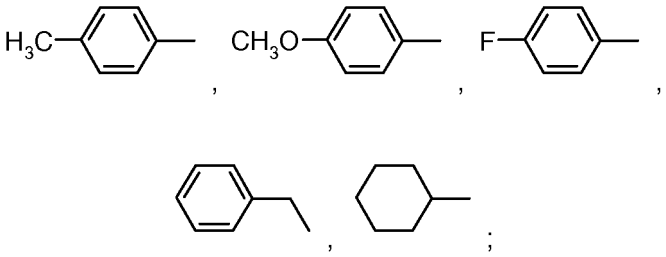


(R = H, Me, Et) by trialkyl phosphite-induced deoxygenation and thermolysis of 1-(o-nitrophenyl)- and 1-(o-azidophenyl)benzimidazoles.

[0003] Pedro Molina et al. Tetrahedron (1994) 10029-10036 reports that aza Wittig-type reaction of bis(iminophosphoranes), derived from bis(2-aminophenyl)amine with two equivalents of isocyanate directly provided benzimidazo[1,2,a]benzimidazole derivatives.

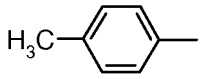


(R = R' =

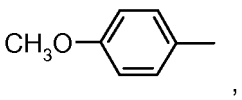


;

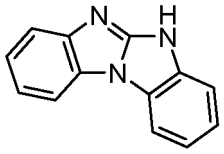
R =



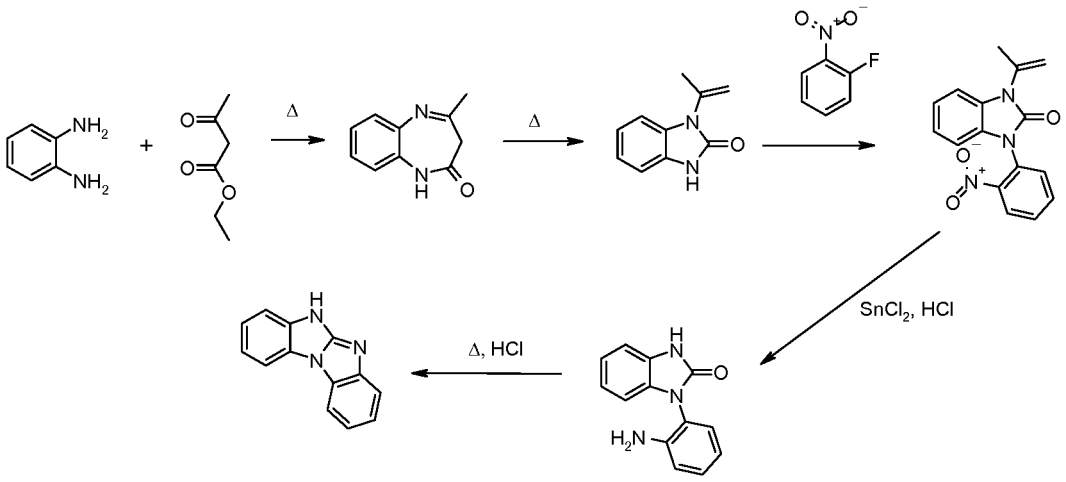
and R' =



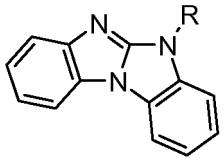
R = iso-propyl and R' = ethyl). The synthesis of



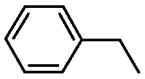
is described, for example, in Achour, Reddouane; Zniber, Rachid, Bulletin des Societes Chimiques Belges 96 (1987) 787-92.



[0004] Hubert, Andre J.; Reimlinger, Hans, Chemische Berichte 103 (1970) 2828-35 describes the synthesis of benzimidazobenzimidazoles

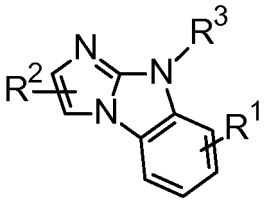


(R = H, CH_3,



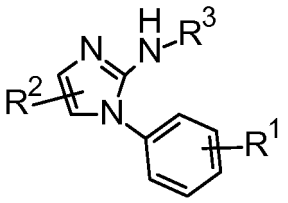
).

[0005] X. Wang et al. Org. Lett. 14 (2012) 452-455 discloses a highly efficient copper-catalyzed synthesis for compounds of formula



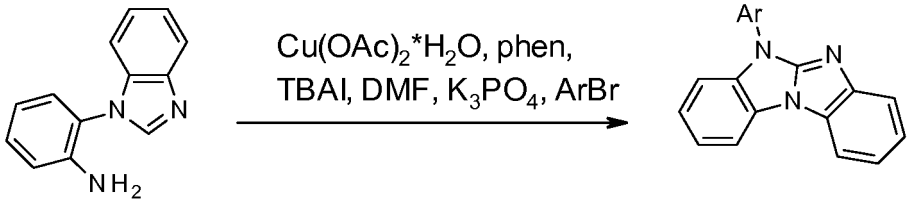
,

wherein compounds of formula

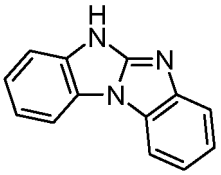


are reacted in the presence of copper acetate ($Cu(OAc)_2$)/PPh_3/1,10-phenathroline/sodium acetate and oxygen in m-xylene (1 atm) at elevated temperature [published on web: December 29, 2011].

[0006] In Eur. J. Org. Chem. 2014, 5986-5997 a new synthesis of benzimidazolo[1,2-a]benzimidazole is described.

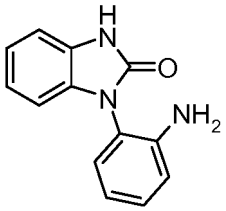


[0007] WO2012/130709 describes a process for the preparation of a compound of formula

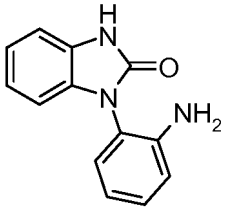


,

which comprises heating a compound of formula



in H_3PO_4, polyphosporic acid, CH_3SO_3H/P_2O_5, CH_3SO_3H, or sulfuric acid. A solvent, or mixtures of solvents having a boiling point above 140 °C, such as, for example, xylene, or mesitylen, may be present. The compound of formula

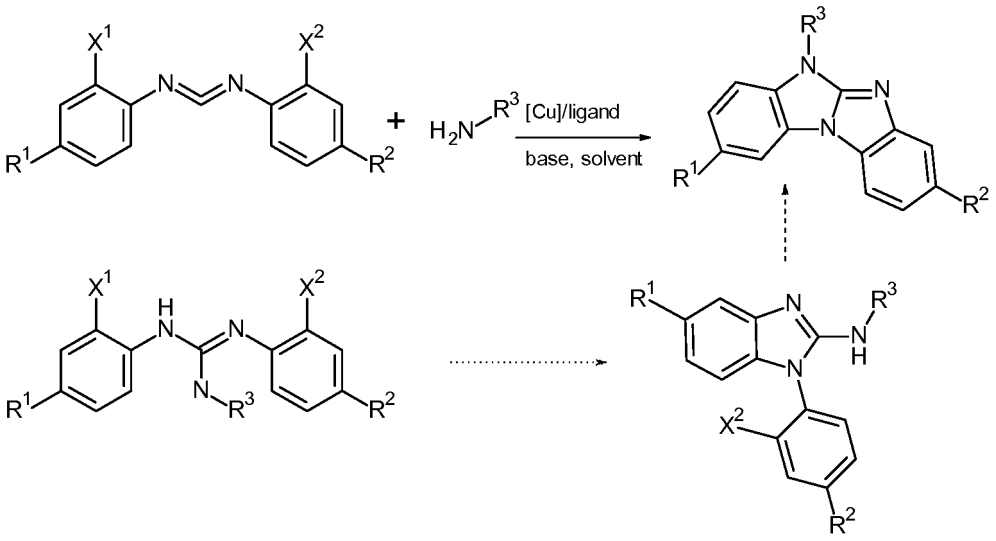


,

the preparation of which is described in Achour, Reddouane; Zniber, Rachid, Bulletin des Societes Chimiques Belges 96 (1987) 787-92, is stirred under an atmosphere of inert gas, such as, for example, nitrogen, or argon, at a temperature above 140 °C, preferably above 160 °C, more preferably above 180 °C, for a time of 30 minutes to 3 weeks, preferably 1 to 48 h.

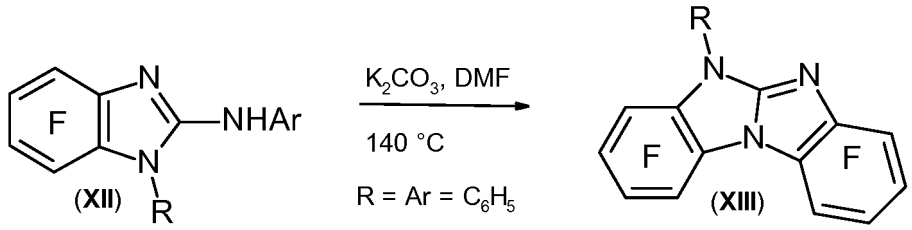
[0008] Guodong Yuan et al., RSC Adv., 2014, 4, 21904 disclose a copper-catalyzed synthesis of benzimidazo[1,2-a]benzimidazoles by domino addition/double cyclization of bis-(o-haloaryl)carbodiimides with primary amines. The pro-

posed mechanism for the domino reaction of bis-(o-haloaryl)carbodiimide with primary amine is shown below:



Compound **3s** (R^1 = H, R^2 = F, R^3 is 2-(5methyl)pyridyl) is obtained with a yield of 80 %.

[0009] I.V. Kolesnikova et al., Journal of Fluorine Chemistry, 40 (1988) 217-246 describes the Synthesis of polyfluorinated carbodiimides, chloroformamidines, guamidines and benzimidazoles. Among others the synthesis of 1,2,3,4,7,8,9,10-octafluoro-5-pentafluorophenyl-5H-benzimidazo[1,2-a]benzimidazole (XIII):

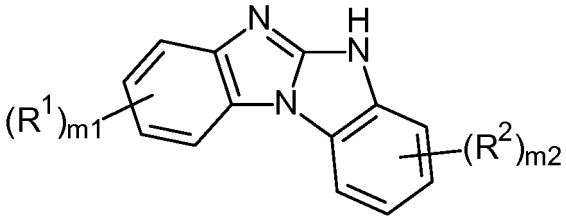


Benzimidazo[1,2-a]benzimidazole derivatives and their use in electronic devices are, for example, described in WO2011/160757, WO2012/130709, WO2013/068376, WO2014/009317, WO2014/044722 and WO2015/014791.

[0010] A novel, concise and efficient method for the synthesis of benzimidazo[1,2-a]benzimidazoles has been developed. The starting materials are readily available, the application scope is broad, and the procedure is convenient.

[0011] The process of the present invention is defined in independent claim 1. Preferred embodiments of the process of the present invention are defined in the dependent claims.

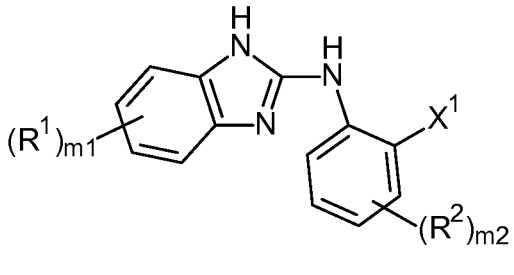
[0012] Disclosed is a process for the preparation of a compound of formula



(I),

comprising

b) heating a compound of formula

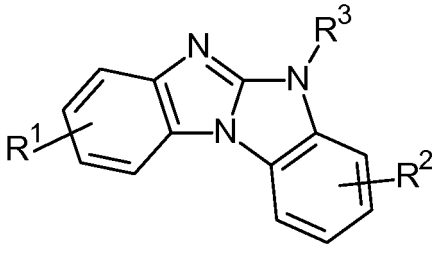


(**II**)

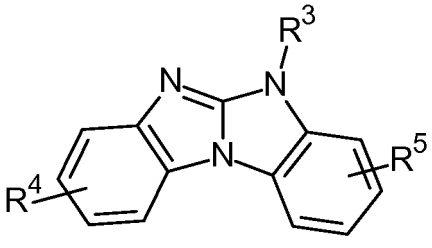
in the presence of a catalyst and a base in a solvent at elevated temperature, wherein

m1 is 0, or an integer 1 to 4, m2 is 0, or an integer 1 to 4,
X^1 is Cl, Br, or I,
R^1 and R^2 are independently of each other a halogen atom, a C_1-C_{25}alkyl group, which can optionally be substituted by E and or interupted by D; a C_1-C_{25}alkoxy group, a group of formula $-(A^5)_v-(A^6)_s-(A^7)_t-(A^8)_u-R^{15}$, $-NR^{10}R^{11}$, or $Si(R^{12})(R^{13})(R^{14})$,
v is 0, or 1, s is 0, or 1, t is 0, or 1, u is 0, or 1,
A^5, A^6, A^7 and A^8 are independently of each other a C_6-C_{24}arylen group, which can optionally be substituted by G, or a C_2-C_{30}heteroarylen group, which can optionally be substituted by G; wherein
R^{10} and R^{11} are independently of each other a C_6-C_{24}aryl group, which can optionally be substituted by G; or a C_2-C_{30}heteroaryl group, which can optionally be substituted by G;
R^{12}, R^{13} and R^{14} are independently of each other a C_1-C_{25}alkyl group, which can optionally be substituted by E and or interupted by D; C_6-C_{24}aryl group, which can optionally be substituted by G; or a C_2-C_{30}heteroaryl group, which can optionally be substituted by G;
R^{15} is a C_6-C_{24}aryl group, which can optionally be substituted by G; or a C_2-C_{30}heteroaryl group, which can optionally be substituted by G;
D is -S-, -SO-, $-SO_2$-, -O-, $-NR^{65}$-, $-SiR^{70}R^{71}$-, $-POR^{72}$-, $-CR^{63}$=CR^{64}-, or -C≡C-,
E is $-OR^{69}$, $-SR^{69}$, $-NR^{65}R^{66}$, $-CONR^{65}R^{66}$, or halogen,
G is E, or a C_1-C_{18}alkyl group, a C_6-C_{24}aryl group, a C_6-C_{24}aryl group, which is substituted by F, C_1-C_{18}alkyl, or C_1-C_{18}alkyl which is interrupted by O; a C_2-C_{30}heteroaryl group, or a C_2-C_{30}heteroaryl group, which is substituted by F, C_1-C_{18}alkyl, or C_1-C_{18}alkyl which is interrupted by O;
R^{63} and R^{64} are independently of each other H, C_6-C_{18}aryl; C_6-C_{18}aryl which is substituted by C_1-C_{18}alkyl, C_1-C_{18}alkoxy; C_1-C_{18}alkyl; or C_1-C_{18}alkyl which is interrupted by -O-;
R^{65} and R^{66} are independently of each other a C_6-C_{18}aryl group; a C_6-C_{18}aryl which is substituted by C_1-C_{18}alkyl, or C_1-C_{18}alkoxy; a C_1-C_{18}alkyl group; or a C_1-C_{18}alkyl group, which is interrupted by -O-; or
R^{65} and R^{66} together form a five or six membered ring,
R^{67} is a C_6-C_{18}aryl group; a C_6-C_{18}aryl group, which is substituted by C_1-C_{18}alkyl, or C_1-C_{18}alkoxy; a C_1-C_{18}alkyl group; or a C_1-C_{18}alkyl group, which is interrupted by -O-,
R^{69} is a C_6-C_{18}aryl; a C_6-C_{18}aryl, which is substituted by C_1-C_{18}alkyl, or C_1-C_{18}alkoxy; a C_1-C_{18}alkyl group; or a C_1-C_{18}alkyl group, which is interrupted by -O-,
R^{70} and R^{71} are independently of each other a C_1-C_{18}alkyl group, a C_6-C_{18}aryl group, or a C_6-C_{18}aryl group, which is substituted by C_1-C_{18}alkyl, and
R^{72} is a C_1-C_{18}alkyl group, a C_6-C_{18}aryl group, or a C_6-C_{18}aryl group, which is substituted by C_1-C_{18}alkyl.

[0013] The compounds of formula (I) are intermediates in the production of compounds of formula



(**VI**), or



(**VIII**).

R^4 is a group of formula $-(A^5)_v-(A^6)_s-(A^7)_t-(A^8)_u-R^{15}$, $-Si(R^{12})(R^{13})(R^{14})$ or $-NR^{10}R^{11}$,

R^5 has the meaning of R^4, or is H, and
R^3 is a group of formula --$(A^1)_o$-$(A^2)_p$-$(A^3)_q$-$(A^4)_r$-R^{16}.

Compound of formula (I)

[0014] R^1 and R^2 are independently of each other a halogen atom, a C_1-C_{25}alkyl group, which can optionally be substituted by E and or interupted by D; a C_1-C_{25}alkoxy group, a group of formula -$(A^5)_v$-$(A^6)_s$-$(A^7)_t$-$(A^8)_u$-R^{15}, -$NR^{10}R^{11}$, or $Si(R^{12})(R^{13})(R^{14})$,

[0015] Halogen is fluorine, chlorine, bromine and iodine.

[0016] Examples of a group of formula $Si(R^{12})(R^{13})(R^{14})$ are a trimethylsilyl group, a triethylsilyl group, a tert-butyldimethylsilyl group, a propyldimethylsilyl group, a triisopropylsilyl group, a triphenylsilyl group, a phenyldimethylsilyl group, a t-butyldiphenylsilyl group, a tritolylsilyl group, a trixylylsilyl group, or a trinaphthylsilyl group.

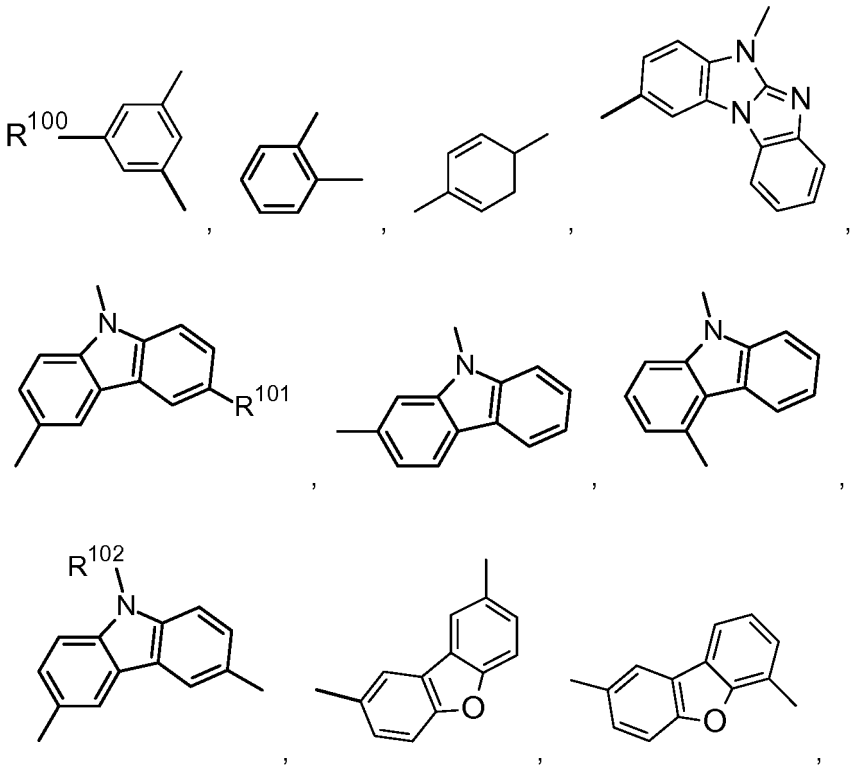
[0017] Examples of the group $N(R^{10})(R^{11})$ include diphenylamino and a phenylnaphthylamino group.

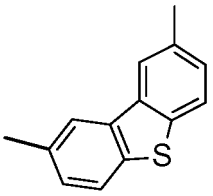
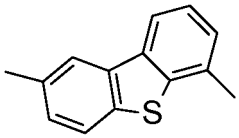
[0018] C_1-C_{25}alkyl (C_1-C_{18}alkyl) is typically linear or branched, where possible. Examples are methyl, ethyl, n-propyl, isopropyl, n-butyl, sec.-butyl, isobutyl, tert.-butyl, n-pentyl, 2-pentyl, 3-pentyl, 2,2-dimethylpropyl, 1,1,3,3-tetramethylpentyl, n-hexyl, 1-methylhexyl, 1,1,3,3,5,5-hexamethylhexyl, n-heptyl, isoheptyl, 1,1,3,3-tetramethylbutyl, 1-methylheptyl, 3-methylheptyl, n-octyl, 1,1,3,3-tetramethylbutyl and 2-ethylhexyl, n-nonyl, decyl, undecyl, dodecyl, tridecyl, tetradecyl, pentadecyl, hexadecyl, heptadecyl, or octadecyl. C_1-C_8alkyl is typically methyl, ethyl, n-propyl, isopropyl, n-butyl, sec.-butyl, isobutyl, tert.-butyl, n-pentyl, 2-pentyl, 3-pentyl, 2,2-dimethyl-propyl, n-hexyl, n-heptyl, n-octyl, 1,1,3,3-tetramethylbutyl and 2-ethylhexyl.

[0019] C_1-C_{25}alkyl may be substituted by one or more E and/or interrupted by one or more units D. E is preferably -OR^{69}; -SR^{69}; -$NR^{65}R^{65}$; -or -$CONR^{65}R^{65}$, wherein R^{65}, R^{67}, R^{68} and R^{69} are independently of each other C_1-C_{18}alkyl, such as methyl, ethyl, n-propyl, iso-propyl, n-butyl, isobutyl, sec-butyl, hexyl, octyl, or 2-ethyl-hexyl, or C_6-C_{14}aryl, such as phenyl, tolyl, naphthyl, or biphenylyl. D is preferably -S-, -SO-, -SO_2-, -O-, -NR^{65}-, wherein R^{65} is C_1-C_{25}alkyl, or C_6-C_{14}aryl, such as phenyl, tolyl, naphthyl, or biphenylyl.

[0020] C_1-C_{25}alkoxy groups (C_1-C_{18}alkoxy groups) are straight-chain or branched alkoxy groups, e.g. methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, sec-butoxy, tert-butoxy, amyloxy, isoamyloxy or tert-amyloxy, heptyloxy, octyloxy, isooctyloxy, nonyloxy, decyloxy, undecyloxy, dodecyloxy, tetradecyloxy, pentadecyloxy, hexadecyloxy, heptadecyloxy and octadecyloxy. Examples of C_1-C_8alkoxy are methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, sec.-butoxy, isobutoxy, tert.-butoxy, n-pentyloxy, 2-pentyloxy, 3-pentyloxy, 2,2-dimethylpropoxy, n-hexyloxy, n-heptyloxy, n-octyloxy, 1,1,3,3-tetramethylbutoxy and 2-ethylhexyloxy.

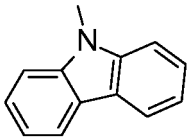
[0021] Examples of the groups A^1, A^2, A^3, A^4, A^5, A^6, A^7 and A^8 are a group of formula




, or 
,

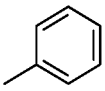
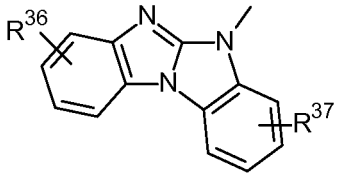
wherein

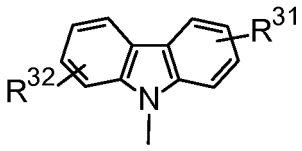
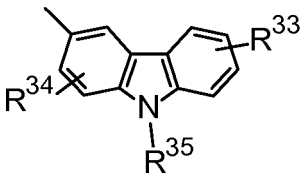
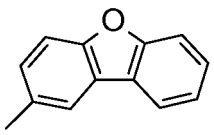
R^{100} is H, $Si(Ph)_3$, or

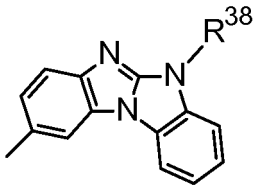
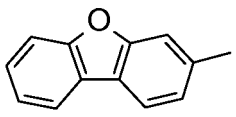
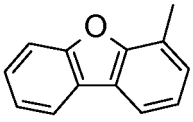
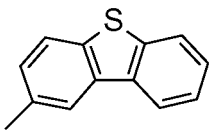

,

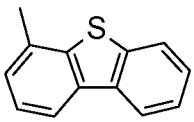
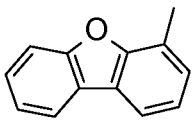
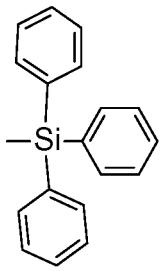
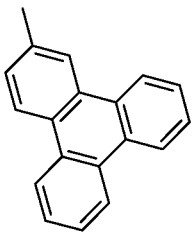
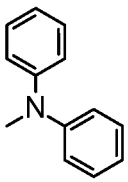
R^{101} is H, or CN,
R^{102} is a phenyl group.

[0022] Examples of R^{15} and R^{16} are a group of formula


, 
,


, 
, 
,


, 
, 
, 
,


, 
, 
, 
and 
.

R^{31}, R^{32}, R^{33}, R^{34}, R^{36} and R^{37} are independently of each other H, or a C_1-C_{25}alkyl group; R^{35} and R^{38} are independently of each a C_6-C_{10}aryl group, which can optionally be substituted by one, or more C_1-C_{25}alkyl groups.

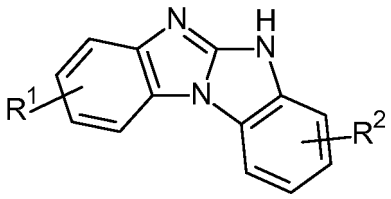
[0023] The groups R^{15} and R^{16} may be substituted by G. G is preferably C_1-C_{18}alkyl, such as methyl, ethyl, n-propyl, iso-propyl, n-butyl, isobutyl, sec-butyl, hexyl, octyl, or 2-ethyl-hexyl; -CF_3, a C_6-C_{14}aryl group, a C_6-C_{14}aryl group, which is substituted by F, or C_1-C_{18}alkyl; a C_2-C_{14}heteroaryl group, or a C_2-C_{14}heteroaryl group, which is substituted by F, or C_1-C_{18}alkyl.

[0024] m1 and m2 are preferably, 0, 1, or 2, more preferably 0, or 1, most preferred 0.

[0025] If m1 is different from 0, R^1 is preferably C_1-C_{25}alkyl, C_1-C_{25}alkoxy, benzyloxy, Br, Cl, or F, more preferably C_1-C_8alkyl, C_1-C_8alkoxy, Br, Cl, or F.

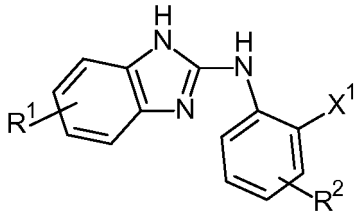
[0026] If m2 is different from 0, R^2 is preferably C_1-C_{25}alkyl, C_1-C_{25}alkoxy, benzyloxy, Br, Cl, or F, more preferably C_1-C_8alkyl, C_1-C_8alkoxy, Br, Cl, or F.

[0027] The compound of formula (I) is preferably a compound of formula



(**Ia**).

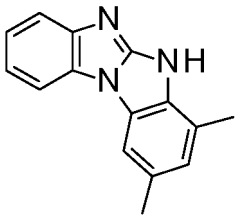
The compound of formula (II) is preferably a compound of formula

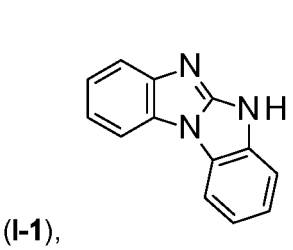
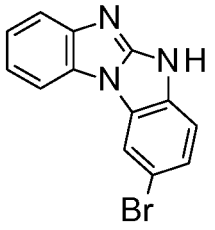
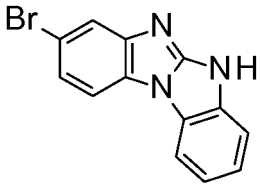


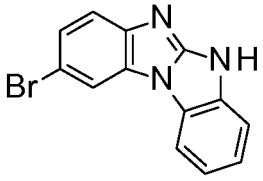
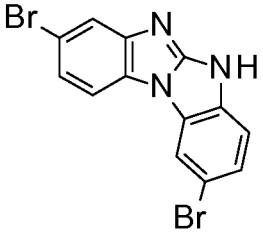
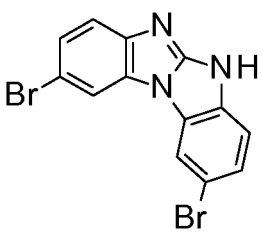
(**IIa**).

X^1 is preferably Cl, Br, or I, R^1 is preferably C_1-C_8alkyl, C_1-C_8alkoxy, Br, Cl, or F, and R^2 is preferably C_1-C_8alkyl, C_1-C_8alkoxy, Br, Cl, or F.

[0028] Most preferred the compound of formula (I) is a compound of formula




(**I-1**),

(**I-2**),

(**I-3**),

(**I-4**),

(**I-5**),

(**I-6**) and

(**I-7**).

The, at present, most preferred compound of formula (I) is compound (**I-2**).

Catalyst:

[0029] The catalyst is preferably a Cu(0) powder, especially a Cu(I) salt, or a Cu(II) salt.

[0030] Preferred Cu(I) salts are selected from CuCl, CuBr, CuI, CuBr-SMe_2, CuSCN, and CuOTf (Cupric trifluoromethane sulfonate). More preferably, the Cu(I) catalyst is selected from CuCl, CuBr, and CuI.

[0031] Preferred Cu(II) salts are selected from $CuBr_2$, $CuCO_3$, $Cu(OAc)_2$, and $Cu(OTf)_2$.

[0032] The amount of Cu, especially Cu(I) and Cu(II) catalyst used depend on the selected starting materials and reaction conditions. Preferably, from 0.01 to 0.20 equivalents of Cu(I) or Cu(II) catalyst are present.

[0033] A ligand may be added for performing the coupling reaction. Examples of ligands used in the Ullmann-coupling reaction would be known to a person of ordinary skill in the art, and can include, without limitation, dimethylethylenediame (DMEDA), tetramethylethylenediamine (TMED), 2,2'-dipyridyl (DPD), triphenylphosphine (TPP), N,N-dimethylglycine (NDMG), tri-t-butylphosphine (tri-tBuP), N-methylglycine, 2,2,4,4-tetramethyl-3,5-heptanedione (TMHD), 8-hydroxyquinoline (HQL), and 1,10-phenanthroline (PNT).

[0034] The amount of ligand present should be approximately equivalent to the amount of Cu catalyst present.

[0035] In a particularly preferred embodiment the catalyst is selected from CuI, and $CuBr_2$ and the catalyst comprises optionally a ligand, especially DMEDA.

[0036] In the most preferred embodiment the catalyst is selected from CuI, and $CuBr_2$ and comprises no ligand.

Base:

[0037] Preferably this base is inorganic and more preferably weak. Though there is no particular limitation, there can be used, for example, alkali metal carbonates, alkali metal hy-drogen-carbonates, alkali metal phosphates, alkali metal hydrogenphosphates and alkali metal dihydrogenphosphates. As the alkali metal carbonates, there can be exemplified sodium carbonate, lithium carbonate, cesium carbonate and potassium carbonate. As the alkali metal phosphates, there can be exemplified sodium phosphate, potassium phosphate, cesium phosphate and lithium phosphate. The alkali metal carbonates, especially K_2CO_3 and Cs_2CO_3, are more preferred. Potassium carbonate is preferred when a polar, aprotic solvent is used. Caesium carbonate is preferred if a less polar organic solvent is used.

[0038] The amount of base is preferably 1.0 to 2.0 molar equivalents, more preferably 1.0 to 1.5 equivalents.

Solvent:

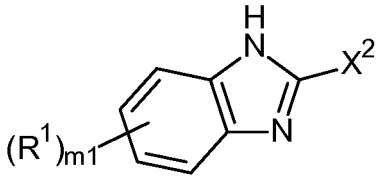
[0039] Preferably, the Ullmann coupling is performed in a suitable polar solvent, or a mixture of suitable polar solvents, which are stable under basic conditions. Suitable polar solvents include, but are not limited to, ether and aprotic solvents. Suitable ether solvents include: 1,2-dimethoxyethane (DME), 1,2-diethoxyethane (DEE), tetrahydrofuran, 1,3-dioxane, 1,4-dioxane, furan, ethylene glycol dimethyl ether, ethylene glycol diethyl ether, diethylene glycol dimethyl ether, diethylene glycol diethyl ether, triethylene glycol dimethyl ether, or t-butyl methyl ether. Suitable aprotic solvents may include, by way of example and without limitation, tetrahydrofuran (THF), dimethylformamide (DMF), dimethylacetamide (DMAC), 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone (DMPU), 1,3-dimethyl-2-imidazolidinone (DMI), N-methylpyrrolidi-

none (NMP), N-methylacetamide, N,N-dimethylacetamide (DMA), N-methylformamide, dimethyl sulfoxide, propionitrile, ethyl formate, hexachloroacetone, sulfolane, N,N-dimethylpropionamide, tetramethylurea, nitromethane, nitrobenzene, or hexamethylphosphoramide.

[0040] Most preferred, the solvent is a solvent which is miscible with water, such as, for example, dimethoxymethane (DME), diethoxyethane (DEE), 1,3-dioxane, 1,4-dioxane, N-methylpyrrolidinone (NMP), N,N-dimethylacetamide (DMA), dimethylformamide (DMF) and mixtures of these solvents.

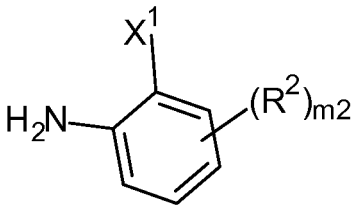
[0041] The Ullmann coupling of is a thermally promoted reaction. Thus, it is preferable to run the coupling reaction under heat. Preferably, the contacting is performed at a temperature of from 100 °C to reflux of the solvent and the reaction is run from 4 to 24 hours.

[0042] Compounds of formula (II) may be obtained by reacting a compound of formula



(**III**)

with a compound of formula



(**IV**)

in the presence of an acid in a solvent at elevated temperature, wherein X^2 is Cl, Br, or I, especially Cl, and m1, m2, R^1, R^2 and X^1 are defined above.

[0043] It is preferable to run the coupling reaction of compound (**III**) and (**IV**) under heat. Preferably, the contacting is performed at a temperature of from 100 °C to reflux of the solvent and the reaction is run from 4 to 24 hours.

Acid:

[0044] The acids include inorganic acids, such as, for example, hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, and phosphoric acid, preferably hydrochloric acid, and sulfuric acid, and organic acids, such as, for example, methane sulfonic acid, campher sulfonic acid, p-toluene sulfonic acid, preferably methane sulfonic acid, campher sulfonic acid, p-toluene sulfonic acid.

[0045] The amount of acid is preferably 1.0 to 2.0 molar equivalents, more preferably 1.0 to 1.5 equivalents.

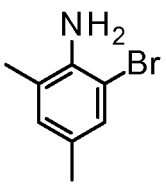
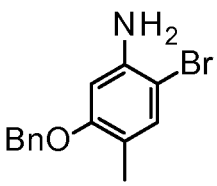
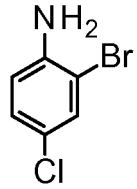
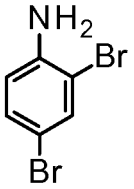
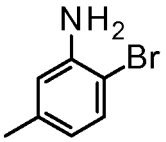
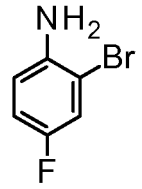
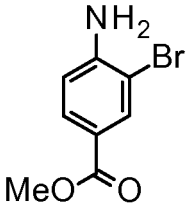
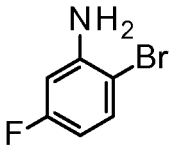
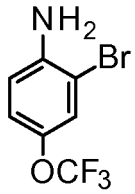
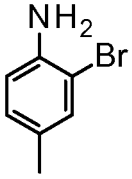
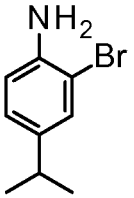
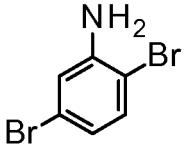
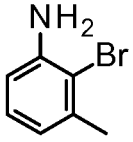
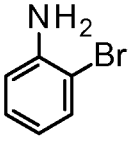
Solvent:

[0046] In principal, step a) can be performed in a suitable aromatic solvent such as, for example, toluene and xylene. Preferably, step a) is performed in a suitable polar solvent, or a mixture of suitable polar solvents, which are stable against acids. Suitable polar solvents include, but are not limited to aprotic solvents. Suitable aprotic solvents may include, by way of example and without limitation, tetrahydrofuran (THF), dimethylformamide (DMF), dimethylacetamide (DMAC), 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone (DMPU), 1,3-dimethyl-2-imidazolidinone (DMI), N-methylpyrrolidinone (NMP), N-methylacetamide, N,N-dimethylacetamide (DMA), N-methylformamide, dimethyl sulfoxide, propionitrile, ethyl formate, hexachloroacetone, sulfolane, N,N-dimethylpropionamide, tetramethylurea, nitromethane, nitrobenzene, or hexamethylphosphoramide.

Most preferred, the solvent is a solvent which is miscible with water, such as, for example, dimethoxymethane (DME), diethoxyethane (DEE), 1,3-dioxane, 1,4-dioxane, N-methylpyrrolidinone (NMP), N,N-dimethylacetamide (DMA), dimethylformamide (DMF) and mixtures of these solvents.

[0047] The compounds of formula **(IV)** are commercially available, or can be produced according to methods known to the person skilled in the art.

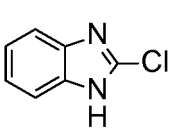
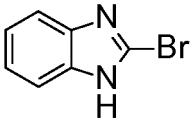
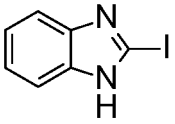
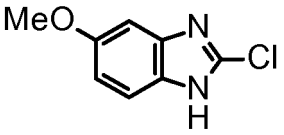
[0048] Examples of commercially available compounds of formula (IV) are shown below:















and

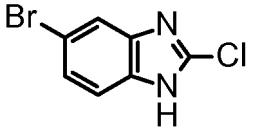
(Bn = benzyl).

The compounds of formula (III) are commercially available, or can be produced according to methods known to the person skilled in the art.

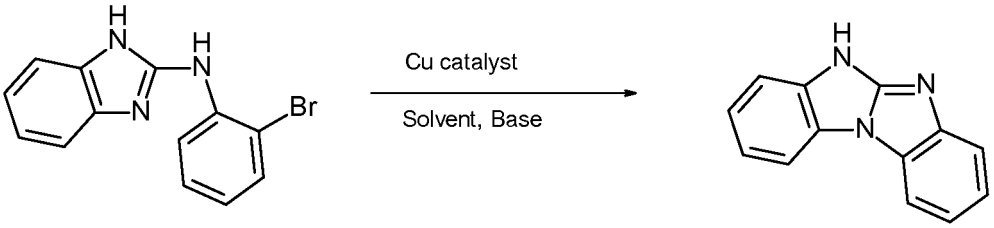
[0049] Examples of commercially available compounds of formula (III) are shown below:

and



[0050] The process of the present invention is illustrated in more detail on basis of the synthesis of 6H-benzimidazolo[1,2-a]benzimidazole, but is not limited thereto.



[0051] The Cu catalyst is preferably CuI, or $CuBr_2$.

[0052] The solvent is preferably 1,4-dioxane, DMF, DMA, NMP, or a mixture of these solvents. Most preferred are DMF, DMA, or NMP. Preferably, from 0.01 to 0.20 equivalents of Cu(I) or Cu(II) catalyst are present.

[0053] The base is preferably K_2CO_3, or $CsCO_3$. The amount of base is preferably 1.0 to 2.0 molar equivalents, more preferably 1.0 to 1.5 equivalents.

[0054] The solvent is preferably a solvent which is miscible with water, such as, for example, 1,3-dioxane, 1,4-dioxane, NMP, DMA, DMF and mixtures of these solvents.

[0055] Preferably, the Ullmann coupling is performed at a temperature of from 100 °C to reflux of the solvent and the reaction is run from 4 to 24 hours.

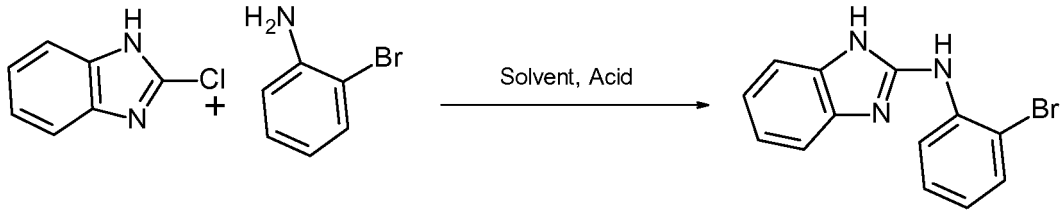
[0056] The currently best results are obtained, when the Ullmann coupling is done in DMF at a temperature of about 130 °C in the presence of a catalytic amount of CuI, or $CuBr_2$ and an excess of caesium carbonate. Under these conditions, cyclization is complete within 4h, proceeds quantitatively and yields reasonably pure material (HPLC ca. 95 area-%) after precipitation by adding water.

[0057] The purity of the crude product can be raised from ca. 95 to above 97.7% by recrystallization in DMF, DMA, or NMP.

[0058] The crude reaction product contains significant amounts of Cu salts. The amount of Cu salts can be decreased by a factor of 2 by reducing the amount of Cu catalyst ($CuBr_2$) from 5 to 2.0 or even 1.0 equivalents.

[0059] The copper content can be further decreased to a level of below 500 ppm and the purity of the product can be increased to more than 99 %, when the crude reaction product is recrystallized in boiling acetic acid.

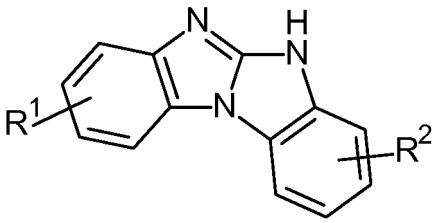
[0060] The required precursor, N-(2-bromophenyl)-1H-benzimidazol-2-amine, can be obtained by reacting 2-chlorobenzimidazole with 2-bromo aniline.



[0061] The currently best results are obtained by reacting 2-chlorobenzimidazole with *o*-bromoaniline in NMP at a temperature of about 100°C in the presence of a stoichiometric amount of methanesulfonic acid. Complete conversion is achieved after 6h. After dilution with water and neutralization with aqueous sodium hydroxide, the precipitated reaction product can be isolated by filtration at room temperature.

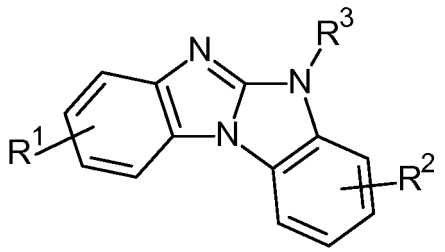
[0062] Benzimidazo[1,2-a]benzimidazole derivatives of formula (I) can be used in electronic devices and/or are starting materials and/or intermediates in the synthesis of materials which can be used in electronic devices. Reference is made, for example, to WO2011/160757, WO2012/130709 (compounds **A-1** to **A-32, B-1** to **B-35, C-1** to **C-78, F-1** to **F-62, G-1** to **G-62),** WO2013/068376 (compounds **A-1** to **A-18, B-1** to **B-18, C-1** to **C-18, D-1** to **D-19, E-1** to **E-6,** WO2014/009317 (compounds **A-1** to **A-51)** and WO2014/044722 **(A-1** to **A-65, B-1** to **B-8, C-1** to **C-65, D-1** to **D-8, E-1** to **E-65,** or **F-1** to **F-65)** and WO2015/014791.

[0063] Accordingly, the process can further comprise reacting c1)



(**Ia**),

with a compound of formula R^3-X^3 **(V),** to obtain a compound of formula

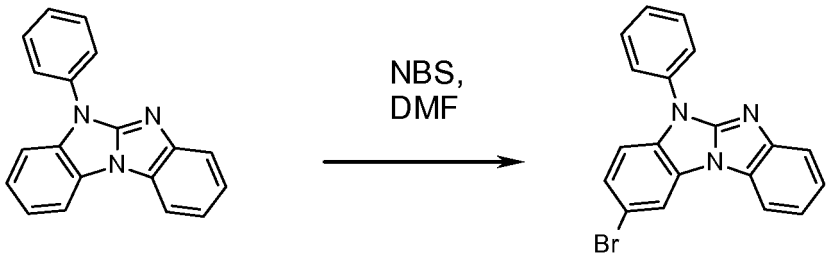


(**VI**),

wherein X^3 is Cl, Br, or I,

R^3 is a group of formula $--(A^1)_o-(A^2)_p-(A^3)_q-(A^4)_r-R^{16}$,
o is 0, or 1, p is 0, or 1, q is 0, or 1, r is 0, or 1,
A^1, A^2, A^3 and A^4 are independently of each other a C_6-C_{24}arylen group, which can optionally be substituted by G, or a C_2-C_{30}heteroarylen group, which can optionally be substituted by G;
R^{16} is a C_6-C_{24}aryl group, which can optionally be substituted by G; or a C_2-C_{30}heteroaryl group, which can optionally be substituted by G; and
R^1, R^2 and G are defined above.

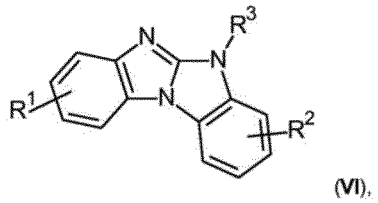
[0064] The bromination of 5-phenylbenzimidazolo[1,2-a]benzimidazole can be carried out in analogy to the bromination of carbazole, which is, for example, described in J. Mater. Chem. 18 (2008) 1296-1301.



[0065] Other bromination methods are, for example, described in Helvetica Chimica Acta 89 (2006) 1123 and SYNLETT 17 (2006) 2841-2845.

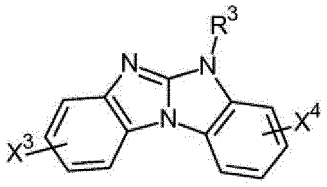
[0066] Halogenation agents for the selective halogenation of benzimidazo[1,2-a]benzimidazole derivatives of formula (I) are available. Examples are N-chlorosuccinimide (NCS) (Synlett 18 (2005) 2837-2842); Br_2 (Synthesis 10 (2005) 1619-1624), N-bromosuccinimide (NBS)(Organic Letters 12 (2010) 2194-2197; Synlett (2006) 2841-2845), 1,3-dibromo-5,5-dimethylhydantoin (DBH) (Organic Process Research & Development 10 (2006) 822-828, US2002/0151456), $CuBr_2$ (Synthetic Communications 37 (2007) 1381-1388); R_4NBr_3 (Can. J. Chem. 67 (1989) 2062), N-iodosuccinimide (NIS)(Synthesis 12 (2001) 1794-1799, J. Heterocyclic Chem. 39 (2002) 933), KI/KIO_3(Org. Lett. 9 (2007) 797, Macromolecules 44 (2011) 1405-1413), $NaO_4/I_2/H_2SO_4$ or $NaIO_4/KI/H_2SO_4$ (J. Heterocyclic Chem. 38 (2001) 77; J. Org. Chem. 75 (2010) 2578-2588); iodine monochloride (ICl; Synthesis (2008) 221-224). Additional methods are described in J. Org. Chem. 74 (2009) 3341-3349; J. Org. Chem. 71 (2006) 7422-7432, Eur. J. Org. Chem. (2008) 1065-1071, Chem. Asian J. 5 (2010) 2162 - 2167, Synthetic. Commun. 28 (1998) 3225.

[0067] Accordingly, the compound of formula



(**VI**),

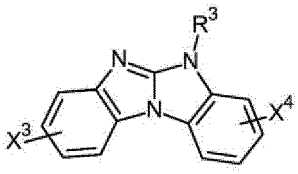
wherein R^1 and R^2 are H, is halogenated to obtain a compound of formula



(VII),

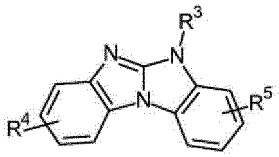
wherein X^3 is Br, or I and X^4 is Br, or I and R^3 is defined above.

[0068] The compound of formula



(VII),

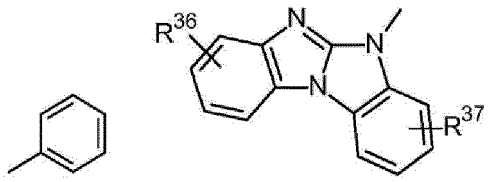
wherein X^3 is Br, or I and X^4 is Br, or I, is transformed to a compound of formula



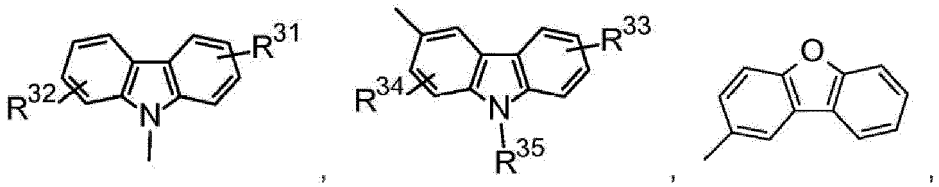
(VIII),

by known methods, wherein R^3 is defined above,

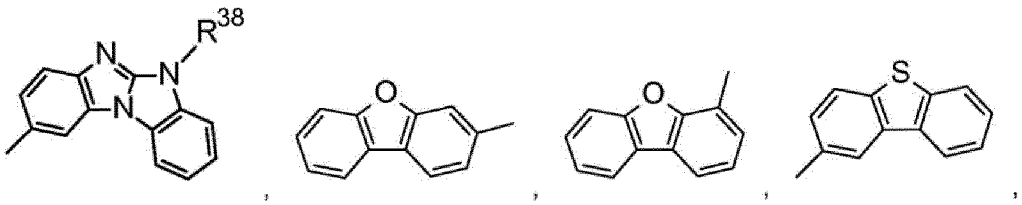
R^4 is a group of formula $-(A^5)_v-(A^6)_s-(A^7)_t-(A^8)_u-R^{15}$, $-Si(R^{12})(R^{13})(R^{14})$ or $-NR^{10}R^{11}$,
R^5 has the meaning of R^4, or is H,
v, s, t, u, A^5, A^6, A^7, A^8, R^{10}, R^{11}, R^{12}, R^{13} and R^{14} are defined above;
R^{15} is a group of formula



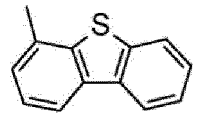
,

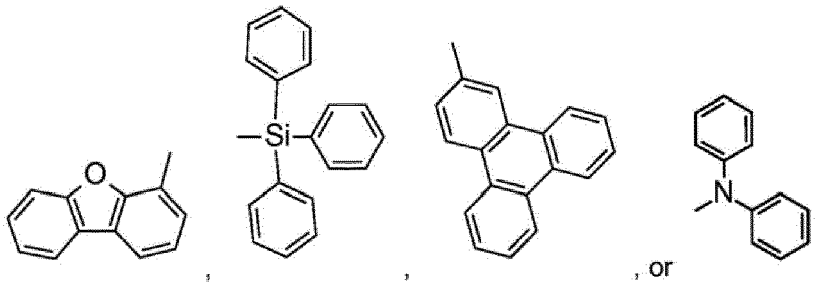


,



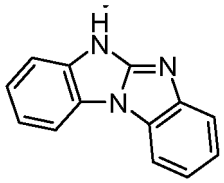
,



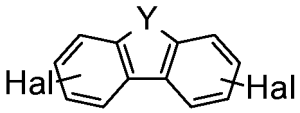


R^{31}, R^{32}, R^{33}, R^{34}, R^{36} and R^{37} are independently of each other H, or a C_1-C_{25}alkyl group;
R^{35} and R^{38} are independently of each a C_6-C_{10}aryl group, which can optionally be substituted by one, or more C_1C_{25}alkyl groups.

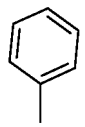
[0069] Heteroarylation can be effected, for example, by copper-catalyzed coupling of

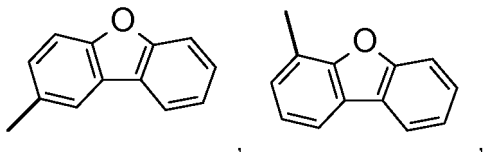


to a halogenated compound of the formula



(Ullmann reaction, Y is O, S, or NY^1, wherein Y^1 is, for example,

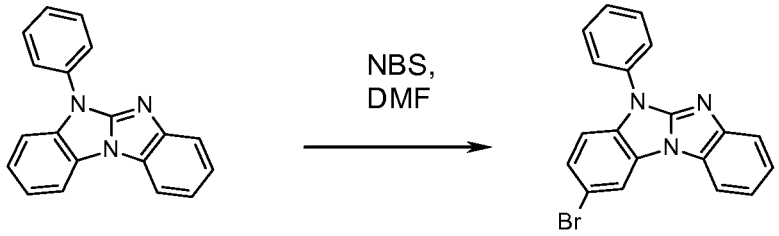




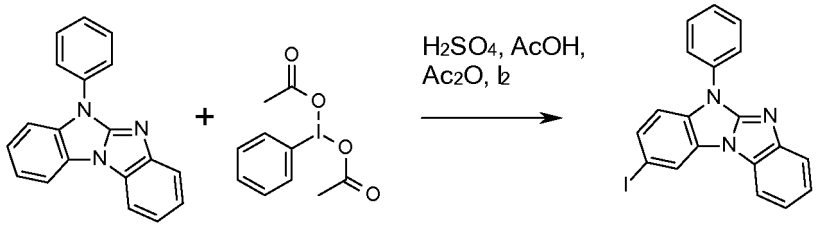
Hal = Cl, Br, or I).

[0070] 5-phenylbenzimidazolo[1,2-a]benzimidazole can be prepared according to example 2a) of WO2014/009317:

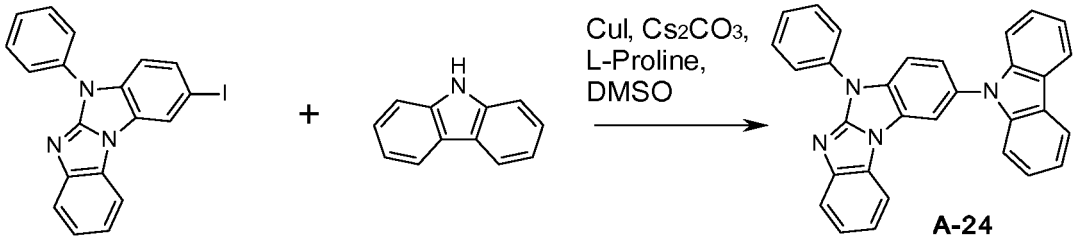
2-bromo-5-phenyl-benzimidazolo[1,2-a]benzimidazole can be prepared according to example 2a) of WO2014/009317:



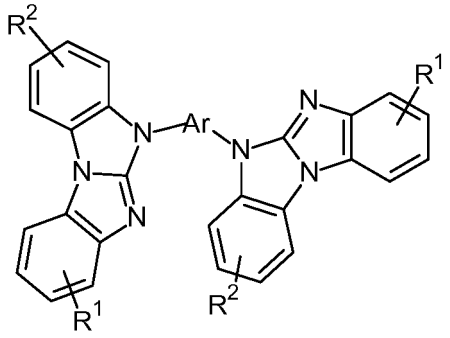
2-iodo-5-phenyl-benzimidazolo[1,2-a]benzimidazole can be prepared according to example 4a) of WO2014/009317:



2-Iodo-5-phenyl-benzimidazolo[1,2-a]benzimidazole can be reacted with carbazole to yield compound **(A-24).** Reference is made to example 4b) of WO2014/009317.

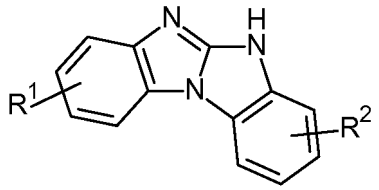


[0071] Compounds of formula



(**X**)

can be obtained by reacting c2) a compound of formula



(I)

with a compound of formula X^5-Ar-X^6 **(IX)**. X^5 and X^6 are independently of each other Cl, Br, or I, Ar is an (hetero)aromatic divalent linking group and R^1 and R^2 are defined above.

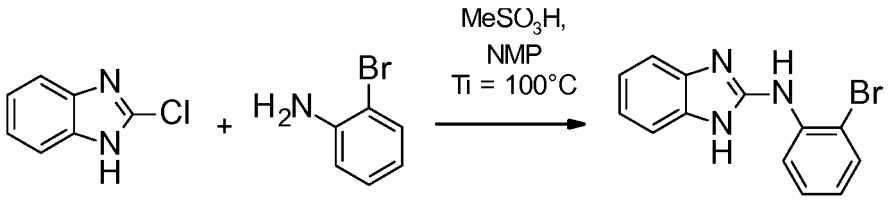
[0072] The following examples are included for illustrative purposes only and do not limit the scope of the claims. Unless otherwise stated, all parts and percentages are by weight.

Examples

Example 1

a) Synthesis of *N*-(2-bromophenyl)-*1H*-benzimidazol-2-amine

[0073]

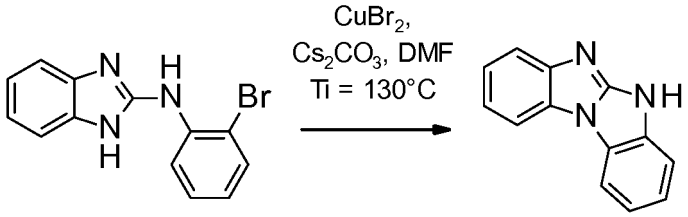


[0074] 2-Chlorobenzimidazole (325.0 g, 2.13 mol) and 2-bromoaniline (403.1, 2.34 mol) are dissolved in NMP (1065mL) at 20°C. Methanesulfonic acid (225.2 g, 2.34 mL) is added dropwise over ca. 0.5 h. The resulting suspension is heated to 100°C and stirred until complete conversion of 2-chlorobenzimidazole. The reaction mixture is then cooled to 20°C, diluted with water (650 mL) and neutralized with 30 w-% aqueous sodium hydroxide (596.4 g, 4.47 mol). The precipitated reaction product is isolated by filtration, washed with water and dried under vacuum at 90°C. *N*-(2-bromophenyl)-*1H*-benzimidazol-2-amine (558.6 g, 91%) is obtained as an off-white amorphous solid, which is used without purification in the ring closure step.

^{1}H-NMR (DMSO-d6): δ = 6.93 (dt, J = 1.1, 7.9 Hz, 1H), 6.99-7.06 (m, 2H), 7.34-7.44 (m, 3H), 7.63 (dd, J = 1.4, 8.0 Hz, 1H), 8.48 (brs, 1H), 8.68 (dd, J = 0.6, 8.1 Hz, 1H), 11.19 (brs, 1H) ppm.

b) Synthesis of 6*H*-benzimidazolo[1,2-a]benzimidazole (I-2)

[0075]



[0076] *N*-(2-bromophenyl)-*1H*-benzimidazol-2-amine 350.0 g, 1.21 mol), cesium carbonate (593.6 g, 1.82 mol) and copper(II) bromide (5.43 g, 0.024 mol) are suspended in DMF (1225 mL). The resulting suspension is heated to 130°C and stirred until complete conversion of *N*-(2-bromophenyl)-*1H*-benzimidazol-2-amine. The reaction mixture is then cooled to 20°C and diluted with water. The precipitated reaction product is isolated by filtration, washed thoroughly with water and dried under vacuum at 100°C. *6H*-benzimidazolo[1,2-a]benzimidazole (243.4 g, 97%) is obtained as an off-white amorphous solid.

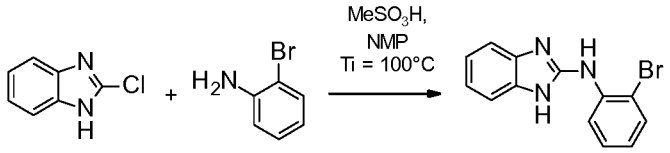
^{1}H-NMR (DMSO-d6): δ = 7.23 (dt, J = 0.8, 7.6 Hz, 2H) 7.30 (dt, J = 0.8, 7.6 Hz, 2H), 7.50 (d, J = 7.6 Hz, 2H), 8.09 (d,

J = 7.6 Hz, 2H), 12.03 (brs, 1H) ppm. **^{13}C-NMR** (DMSO-d6): δ = 111.2, 115.0, 120.3, 123.3, 126.6, 141.6, 153.8 ppm.

Example 2

a) Synthesis of *N*-(2-bromophenyl)-*1H*-benzimidazol-2-amine

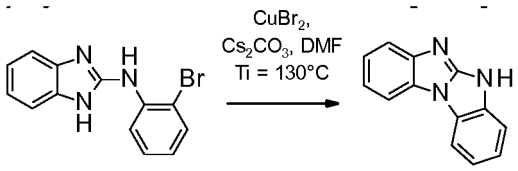
[0077]



[0078] 2-Chlorobenzimidazole (325.0 g, 2.13 mol) and 2-bromoaniline (403.1 g, 2.34 mol) are dissolved in NMP (1065 mL) at 20°C. Methanesulfonic acid (225.2 g, 2.34 mL) is added dropwise over ca. 0.5 h. The resulting suspension is heated to 100°C and stirred until complete conversion of 2-chlorobenzimidazole. The reaction mixture is then cooled to 20°C, diluted with water (650 mL) and neutralized with 30 w-% aqueous sodium hydroxide (596.4 g, 4.47 mol). The precipitated reaction product is isolated by filtration, washed with water and dried under vacuum at 90°C. *N*-(2-bromophenyl)-*1H*-benzimidazol-2-amine (558.6 g, 91%) is obtained as an off-white amorphous solid, which was used without purification in the ring closure step.
1H-NMR (DMSO-d6): δ = 6.93 (dt, J = 1.1, 7.9 Hz, 1H), 6.99-7.06 (m, 2H), 7.34-7.44 (m, 3H), 7.63 (dd, J = 1.4, 8.0 Hz, 1H), 8.48 (brs, 1H), 8.68 (dd, J = 0.6, 8.1 Hz, 1H), 11.19 (brs, 1H) ppm.

b) Synthesis of *6H*-benzimidazolo[1,2-a]benzimidazole (I-2)

[0079]

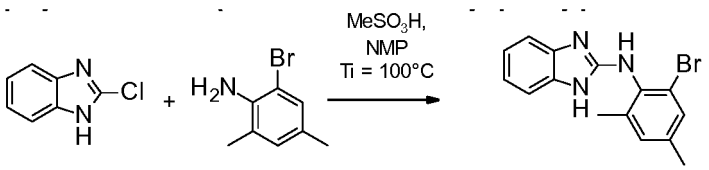


[0080] *N*-(2-bromophenyl)-*1H*-benzimidazol-2-amine (350.0 g, 1.21 mol), cesium carbonate (593.6 g, 1.82 mol) and copper(II) bromide (5.43 g, 0.024 mol) are suspended in DMF (1225 mL). The resulting suspension is heated to 130°C and stirred until complete conversion of *N*-(2-bromophenyl)-*1H*-benzimidazol-2-amine. The reaction mixture is then cooled to 20°C and diluted with water. The precipitated reaction product is isolated by filtration, washed thoroughly with water and dried under vacuum at 100°C. *6H*-benzimidazolo[1,2-a]benzimidazole (243.4 g, 97%) is obtained as an off-white amorphous solid, which is further purified by recrystallization from acetic acid.
1H-NMR (DMSO-d6): δ = 7.23 (dt, J = 0.8, 7.6 Hz, 2H), 7.30 (dt, J = 0.8, 7.6 Hz, 2H), 7.50 (d, J = 7.6 Hz, 2H), 8.09 (d, J = 7.6 Hz, 2H), 12.03 (brs, 1H) ppm. **13C-NMR** (DMSO-d6): δ = 111.2, 115.0, 120.3, 123.3, 126.6, 141.6, 153.8 ppm.

Example 3

a) Synthesis of *N*-(2-bromo-4,6-dimethyl-phenyl)-*1H*-benzimidazol-2-amine

[0081]



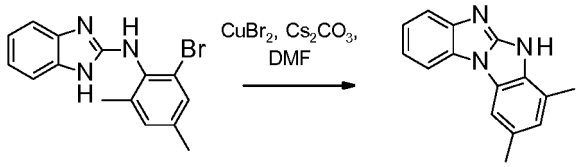
[0082] 2-Chlorobenzimidazole (6.9 g, 45.4 mmol) and 2-bromo-4,6-dimethylaniline (10.0 g, 50.0 mmol) are dissolved

in NMP (23 mL) at 20°C. Methanesulfonic acid (4.8 g, 50.0 mmol) is added dropwise over ca. 0.5 h. The resulting suspension is heated to 100°C and stirred until complete conversion of 2-chlorobenzimidazole. The reaction mixture is then cooled to 20°C, diluted with water (14 mL) and neutralized with 30 w-% aqueous sodium hydroxide (12.7 g, 95.3 mmol). The precipitated reaction product is isolated by filtration, washed with water and dried under vacuum at 90°C. Crude *N*-(2-bromo-4,6-dimethyl-phenyl)-*1H*-benzimidazol-2-amine (10.3 g, 72%) is obtained as an off-white amorphous solid, which was further purified by recrystallization from methanol.

1H-NMR (DMSO-d6): δ = 2.21 (s, 3H), 2.31 (s, 3H), 6.83-6.95 (m, 2H), 7.06-7.18 (m, 3H), 7.39 (brs, 1H), 8.58 (brs, 1H), 10.75 (brs, 1H) ppm.

b) Synthesis of 2,4-dimethyl-*5H*-benzimidazolo[1,2-a]benzimidazole (I-1)

[0083]



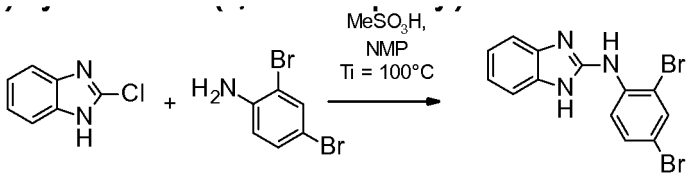
[0084] *N*-(2-bromo-4,6-dimethyl-phenyl)-*1H*-benzimidazol-2-amine (5.8 g, 18.2 mmol), cesium carbonate (8.9 g, 27.3 mmol) and copper(II) bromide (81.2 mg, 0.36 mmol) are suspended in DMF (18 mL). The resulting suspension is heated to 130°C and stirred until complete conversion of *N*-(2-bromo-4,6-dimethyl-phenyl)-*1H*-benzimidazol-2-amine. The reaction mixture is then cooled to 20°C and diluted with water. The precipitated reaction product is isolated by filtration, washed thoroughly with water and dried under vacuum at 100°C. Crude 2,4-dimethyl-*5H*-benzimidazolo[1,2-a]benzimidazole (3.9 g, 91%) is obtained as an off-white amorphous solid, which was further purified by recrystallization from acetic acid.

1H-NMR (DMSO-d6): δ = 2.46 (s, 3H), 2.48 (s, 3H), 6.95 (brs, 1H), 7.20 (dt, J = 1.0, 7.7 Hz, 1H), 7.27 (dt, J = 1.0, 7.6 Hz, 1H), 7.51 (d, J = 7.8 Hz, 1H), 7.74 (brs, 1H), 8.04 (d, J = 7.6 Hz, 1H), 11.85 (brs, 1H) ppm. **13C-NMR** (DMSO-d6): δ = 17.0, 21.5, 109.0, 111.0, 115.6, 119.9, 123.1, 123.4, 125.3, 126.0, 127.0, 129.8, 136.9 (brs), 143.3 (brs), 153.7 ppm. The molecular ions identified in positive ESI-MS at **m/z** 236 $[M + H]^+$ allowed the deduction of its molecular weight of 235 g mol^{-1}.

Example 4

a) Synthesis of *N*-(2,4-dibromophenyl)-*1H*-benzimidazol-2-amine

[0085]

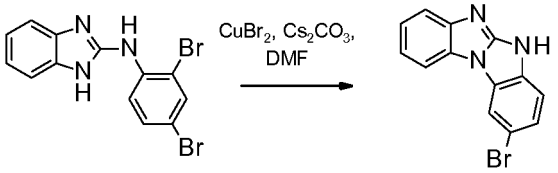


[0086] 2-Chlorobenzimidazole (13.9 g, 90.8 mmol) and 2,4-dibromoaniline (25.1 g, 99.9 mmol) ire dissolved in NMP (45 mL) at 20°C. Methanesulfonic acid (9.6 g, 99.9 mmol) is added dropwise over ca. 0.5 h. The resulting suspension is heated to 100°C and stirred until complete conversion of 2-chlorobenzimidazole. The reaction mixture is then cooled to 20°C, diluted with water (28 mL) and neutralized with 30 w-% aqueous sodium hydroxide (25.4 g, 190.5 mmol). The precipitated reaction product is isolated by filtration, washed with water and dried under vacuum at 90°C. Crude *N*-(2,4-dibromophenyl)-*1H*-benzimidazol-2-amine (33.6 g, 100%) is obtained as an off-white amorphous solid, which is further purified by recrystallization from methanol.

1H-NMR (DMSO-d6): δ = 6.99-7.11 (m, 2H), 7.34-7.44 (m, 2H), 7.61 (dd, J = 2.3, 8.9 Hz, 1H), 7.84 (d, J = 2.3 Hz, 1H), 8.69 (d, J = 8.9 Hz, 1H), 8.69 (brs, 1H), 11.16 (brs, 1H) ppm.

b) Synthesis of 2-bromo-*5H*-benzimidazolo[1,2-a]benzimidazole (I-3)

[0087]

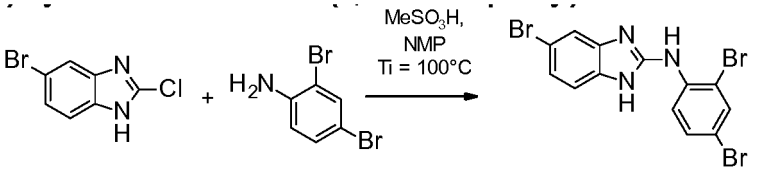


[0088] A suspension of cesium carbonate (13.3 g, 40.9 mmol) and copper(II) bromide (121.7 mg, 0.54 mmol) in DMF (48 mL) is heated to 130°C. A solution of *N*-(2,4-dibromophenyl)-*1H*-benzimidazol-2-amine (10.0 g, 27.2 mmol) in DMF (20 mL) is added dropwise over ca. 2 h. After complete conversion of *N*-(2,4-dibromophenyl)-*1H*-benzimidazol-2-amine, the reaction mixture is cooled to 20°C and diluted with water. The precipitated reaction product is isolated by filtration, washed thoroughly with water and dried under vacuum at 100°C. Crude 2-bromo-*5H*-benzimidazolo[1,2-a]benzimidazole (7.9 g, 100%) is obtained as an off-white amorphous solid, which was further purified by recrystallization from DMF.
1H-NMR (DMSO-d6): δ = 7.26 (t, J = 7.6 Hz, 1H), 7.33 (t, J = 7.6 Hz, 1H), 7.38-7.60 (m, 3H), 8.22 (d, J = 7.7 Hz, 1H), 8.41 (brs, 1H), 12.18 (brs, 1H) ppm. **13C-NMR** (DMSO-d6): δ = 111.6, 111.8, 113.7, 114.0, 117.8, 120.0, 120.9, 123.9, 125.8, 128.2, 138.7 (brs), 143.6 (brs), 154.1 ppm. The molecular ions identified in positive ESI-MS at **m/z** 286 $[M + H]^+$ and **m/z** 288 $[M + H]^+$ allowed the deduction of its molecular weight of 286 g mol^{-1}.

Example 5

a) Synthesis of 5-bromo-*N*-(2,4-dibromophenyl)-*1H*-benzimidazol-2-amine

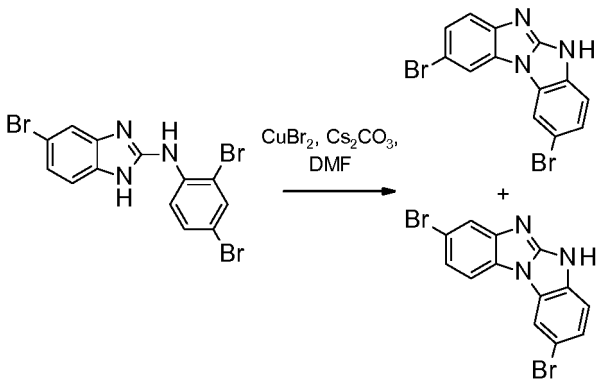
[0089]



[0090] 5-Bromo-2-chloro-*1H*-benzimidazole (10.0 g, 43.2 mmol) and 2,4-dibromoaniline (11.9 g, 47.5 mmol) are dissolved in NMP (22 mL) at 20°C. Methanesulfonic acid (4.6 g, 47.5 mmol) is added dropwise over ca. 0.5 h. The resulting suspension is heated to 100°C and stirred until complete conversion of 5-Bromo-2-chloro-*1H*-benzimidazole. The reaction mixture is then cooled to 20°C, diluted with water (13 mL) and neutralized with 30 w-% aqueous sodium hydroxide (12.1 g, 90.8 mmol). The mixture is diluted with ethyl acetate (150 mL) and the aqueous phase separated. The organic phase is extracted with water (3 $\times$ 50 mL), dried over anhydrous sodium sulphate and evaporated to dryness. Crude 5-bromo-N-(2,4-dibromophenyl)-*1H*-benzimidazol-2-amine (23.5 g) is obtained as an off-white amorphous solid, which is further purified by recrystallization from methanol.
1H-NMR (DMSO-d6): δ = 7.17 (dd, J = 1.9, 8.4 Hz, 1H), 7.34 (d, J = 8.4 Hz, 1H), 7.58 (brs, 1H), 7.61 (dd, J = 2.3, 8.9 Hz, 1H), 7.86 (d, J = 2.3 Hz, 1H), 8.60 (d, J = 8.5 Hz, 1H), 8.76 (brs, 1H), 11.31 (brs, 1H) ppm.

b) Synthesis of 2,9- and 3,9-dibromo-*6H*-benzimidazolo[1,2-a]benzimidazole (I-6) & (I-7)

[0091]

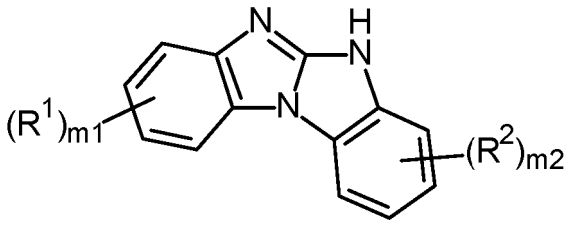


[0092] A suspension of cesium carbonate (11.2 g, 34.5 mmol) and copper(II) bromide (102.7 mg, 0.46 mmol) in DMF (39 mL) is heated to 130°C. A solution of 5-bromo-*N*-(2,4-dibromophenyl)-*1H*-benzimidazol-2-amine (10.3 g, 23.0 mmol) in DMF (18 mL) is added dropwise over ca. 1 h. After complete conversion of 5-bromo-*N*-(2,4-dibromophenyl)-*1H*-benzimidazol-2-amine, the reaction mixture is cooled to 20°C and diluted with water. The precipitated reaction product is isolated by filtration, washed thoroughly with water and dried under vacuum at 100°C. Crude reaction product (4.5 g, 53%) is obtained as an off-white amorphous solid (mixture of isomers), which is further purified by recrystallization from acetic acid.

[0093] The molecular ions identified in positive ESI-MS at **m/z** 364 $[M + H]^+$, **m/z** 366 $[M + H]^+$ and **m/z** 368 $[M + H]^+$ allowed the deduction of its molecular weight of 365 g mol^{-1}.

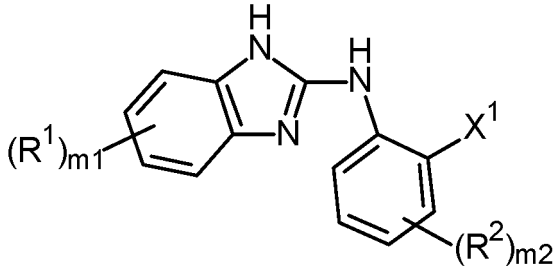
Claims

1. A process for the preparation of a compound of formula



(**I**),

comprising heating a compound of formula



(II) in the presence of a catalyst and a base in a solvent at elevated temperature, wherein

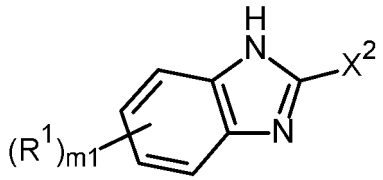
m1 is 0, 1, or 2, m2 is 0, 1 or 2,
X^1 is Cl, Br, or I, and
R^1 and R^2 are independently of each other C_1-C_{25}alkyl, C_1-C_{25}alkoxy, benzyloxy, Br, Cl, or F, preferably C_1-C_8alkyl, C_1-C_8alkoxy, Br, Cl, or F.

2. The process according to claim 1, wherein the catalyst is selected from CuI, and $CuBr_2$ and the catalyst comprises optionally a ligand, especially dimethylethylenediamine.

3. The process according to claim 1, or 2, wherein the base is selected from Cs_2CO_3, and K_2CO_3.

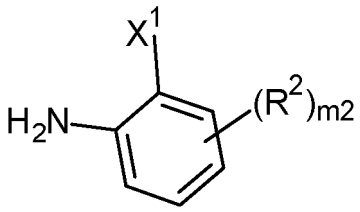
4. The process according to any of claims 1 to 3, wherein the solvent is selected from dimethoxymethane, diethoxyethane, 1,3-dioxane, 1,4-dioxane, N-methylpyrrolidinone, N,N-dimethylacetamide, dimethylformamide, and mixtures of these solvents.

5. The process according to any of claims 1 to 4, comprising reacting a compound of formula



(**III**)

with a compound of formula



(**IV**)

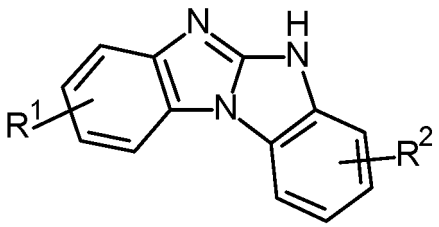
in the presence of an acid in a solvent at elevated temperature to obtain a compound of formula (**II**), wherein

X^2 is Cl, Br, or I, especially Cl, and
m1, m2, R^1, R^2 and X^1 are defined in claim 1.

6. The process according to claim 5, wherein the acid is selected from methane sulfonic acid, campher sulfonic acid, p-toluene sulfonic acid hydrochloric acid, and sulfuric acid.

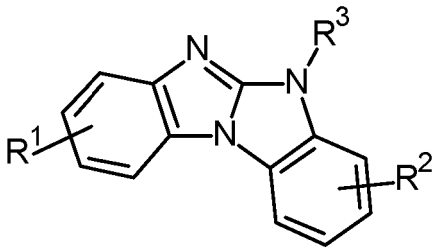
7. The process according to claim 5, or 6, wherein the solvent is selected from dimethoxymethane, diethoxyethane, 1,3-dioxane, 1,4-dioxane, N-methylpyrrolidinone, N,N-dimethylacetamide, dimethylformamide, and mixtures of these solvents.

8. The process according to any of claims 1 to 7, which further comprises reacting c1)



(**Ia**),

with a compound of formula R^3-X^3 (**V**), to obtain a compound of formula

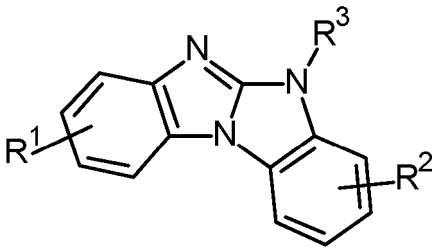


(**VI**),

wherein X^3 is Cl, Br, or I,

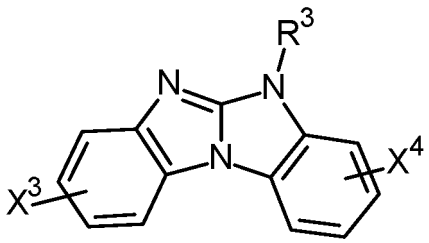
R^3 is a C_6-C_{24}aryl group or a C_2-C_{30}heteroaryl group; and
R^1 and R^2 are defined in claim 1.

9. The process according to claim 8, wherein the compound of formula



(**VI**),

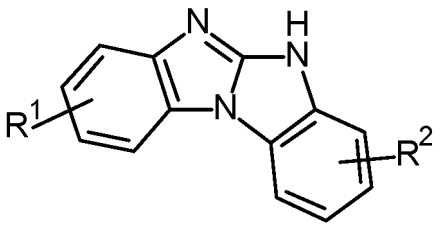
wherein R^1 and R^2 are H, is halogenated to obtain a compound of formula



(**VII**),

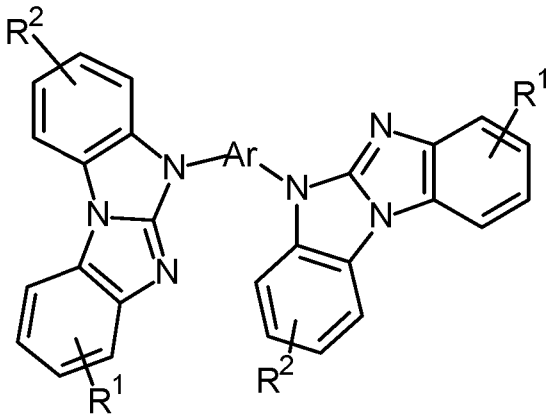
wherein X^3 is Br, or I and X^4 is Br, or I and R^3 is defined in claim 8.

10. The process according to any of claims 1 to 7, which further comprises reacting c2)



(**I**),

with a compound of formula X^5-Ar-X^6 (**IX**), to obtain a compound of formula

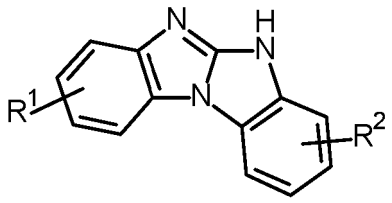


(**X**),

wherein X^5 and X^6 are independently of each other Cl, Br, or I, Ar is an (hetero)aromatic divalent linking group and R^1 and R^2 are defined in claim 1.

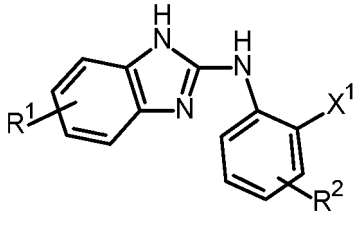
11. The process according to any of claims 1 to 8, wherein m1 and m2 are 0.

12. The process according to any of claims 1 to 8, wherein the compound of formula (I) is a compound of formula



(**Ia**)

and the compound of formula (II) is a compound of formula



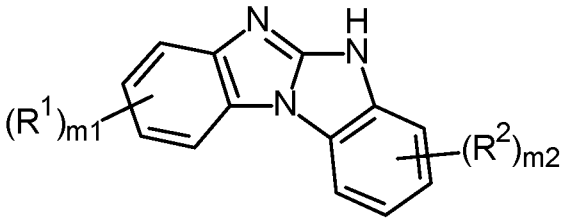
(**IIa**),

wherein

X^1 is Cl, Br, or I,
R^1 is C_1-C_8alkyl, C_1-C_8alkoxy, Br, Cl, or F, and
R^2 is C_1-C_8alkyl, C_1-C_8alkoxy, Br, Cl, or F.

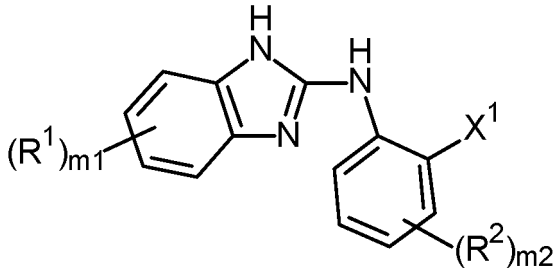
Patentansprüche

1. Ein Verfahren zur Herstellung einer Verbindung der Formel



(I),

umfassend Erhitzen einer Verbindung der Formel



(II)

in Gegenwart eines Katalysators und einer Base in einem Lösungsmittel bei erhöhter Temperatur, wobei

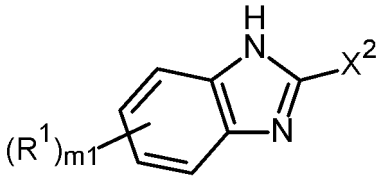
m1 0, 1 oder 2 ist, m2 0, 1 oder 2 ist,
X^1 Cl, Br oder I ist, und
R^1 und R^2 unabhängig voneinander C_1-C_{25}-Alkyl, C_1-C_{25}-Alkoxy, Benzyloxy, Br, Cl oder F, vorzugsweise C_1-C_8-Alkyl, C_1-C_8-Alkoxy, Br, Cl oder F, sind.

2. Das Verfahren nach Anspruch 1, wobei der Katalysator ausgewählt ist aus CuI und $CuBr_2$ und der Katalysator optional einen Liganden, insbesondere Dimethylethylendiamin, umfasst.

3. Das Verfahren nach Anspruch 1 oder 2, wobei die Basis ausgewählt ist aus Cs_2CO_3 und K_2CO_3.

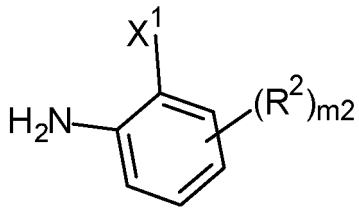
4. Das Verfahren nach einem der Ansprüche 1 bis 3, wobei das Lösungsmittel ausgewählt ist aus Dimethoxymethan, Diethoxyethan, 1,3-Dioxan, 1,4-Dioxan, N-Methylpyrrolidinon, N,N-Dimethylacetamid, Dimethylformamid und Mischungen dieser Lösungsmittel.

5. Das Verfahren nach einem der Ansprüche 1 bis 4, umfassend Umsetzen einer Verbindung der Formel



(III)

mit einer Verbindung der Formel



(**IV**)

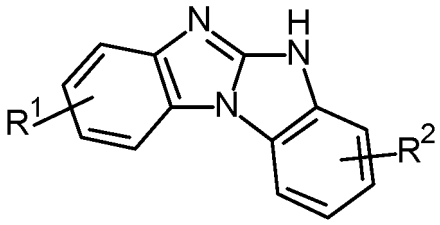
in Gegenwart einer Säure in einem Lösungsmittel bei erhöhter Temperatur, um eine Verbindung der Formel (**II**) zu erhalten, wobei

X^2 Cl, Br oder I, insbesondere Cl, ist und
m1, m2, R^1, R^2 und X^1 wie in Anspruch 1 definiert sind.

6. Das Verfahren nach Anspruch 5, wobei die Säure ausgewählt ist aus Methansulfonsäure, Camphersulfonsäure, p-Toluolsulfonsäure, Salzsäure und Schwefelsäure.

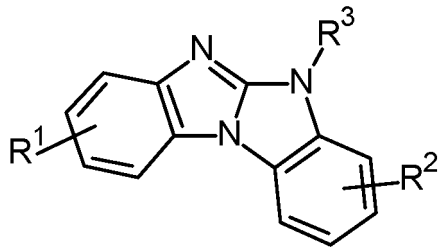
7. Das Verfahren nach Anspruch 5 oder 6, wobei das Lösungsmittel ausgewählt ist aus Dimethoxymethan, Diethoxyethan, 1,3-Dioxan, 1,4-Dioxan, N-Methylpyrrolidinon, N,N-Dimethylacetamid, Dimethylformamid und Mischungen dieser Lösungsmittel.

8. Das Verfahren nach einem der Ansprüche 1 bis 7, weiterhin umfassend das Umsetzen von c1)



(**Ia**),

mit einer Verbindung der Formel R^3-X^3 (V), um eine Verbindung der Formel

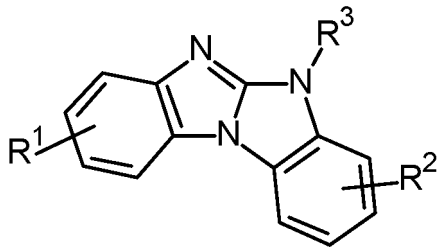


(**VI**)

zu erhalten, wobei X^3 Cl, Br oder I ist,

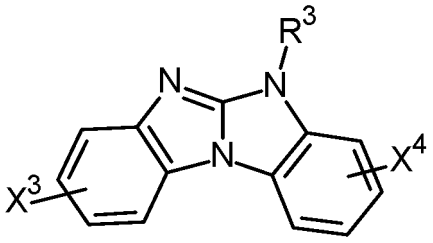
R^3 eine C_6-C_{24}-Arylgruppe oder eine C_2-C_{30}-Heteroarylgruppe ist; und
R^1 und R^2 wie in Anspruch 1 definiert sind.

9. Das Verfahren nach Anspruch 8, wobei die Verbindung der Formel



(**VI**),

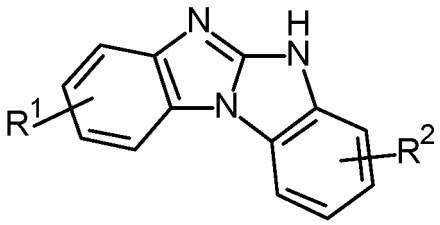
wobei R^1 und R^2 H sind, halogeniert wird, um eine Verbindung der Formel



(**VII**)

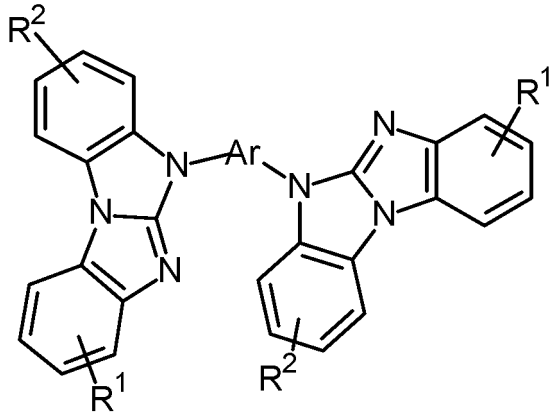
zu erhalten, wobei X^3 Br oder I ist und X^4 Br oder I ist und R^3 wie in Anspruch 8 definiert ist.

10. Das Verfahren nach einem der Ansprüche 1 bis 7, weiterhin umfassend das Umsetzen von c2)



(**I**),

mit einer Verbindung der Formel X^5-Ar-X^6 (**IX**), um eine Verbindung der Formel

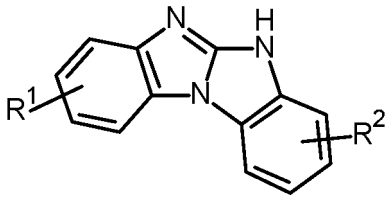


(**X**)

zu erhalten, wobei X^5 und X^6 unabhängig voneinander Cl, Br oder I sind, Ar eine (hetero)aromatische zweiwertige Verbindungsgruppe ist und R^1 und R^2 wie in Anspruch 1 definiert sind.

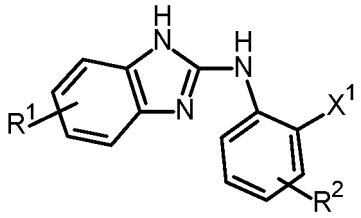
11. Das Verfahren nach einem der Ansprüche 1 bis 8, wobei m1 und m2 0 sind.

12. Das Verfahren nach einem der Ansprüche 1 bis 8, wobei die Verbindung der Formel (I) eine Verbindung der Formel



(**Ia**)

ist und die Verbindung der Formel (**II**) eine Verbindung der Formel

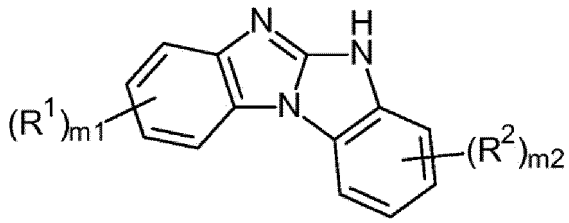


(**IIa**) ist, wobei

X^1 Cl, Br oder I ist,
R^1 C_1-C_8-Alkyl, C_1-C_8-Alkoxy, Br, Cl oder F ist und
R^2 C_1-C_8-Alkyl, C_1-C_8-Alkoxy, Br, Cl oder F ist.

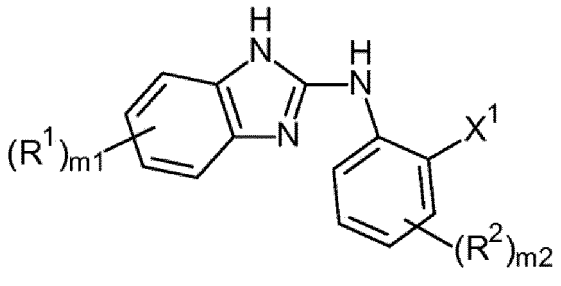
Revendications

1. Procédé pour la préparation d'un composé de formule



(**I**),

comprenant le chauffage d'un composé de formule



(**II**)

en présence d'un catalyseur et d'une base dans un solvant à température élevée, où

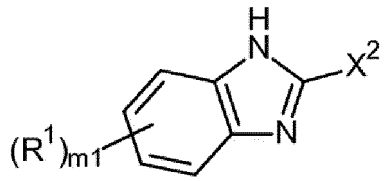
m1 est 0, 1 ou 2, m2 est 0, 1 ou 2,
X^1 est Cl, Br ou I, et
R^1 et R^2 sont, indépendamment l'un de l'autre, alkyle en C_1-C_{25}, alcoxy en C_1-C_{25}, benzyloxy, Br, Cl ou F, de préférence alkyle en C_1-C_8, alcoxy en C_1-C_8, Br, Cl ou F.

2. Procédé selon la revendication 1, où le catalyseur est sélectionné parmi CuI et $CuBr_2$ et le catalyseur comprend facultativement un ligand, en particulier la diméthyléthylènediamine.

3. Procédé selon la revendication 1 ou 2, où la base est sélectionnée parmi Cs_2CO_3 et K_2CO_3.

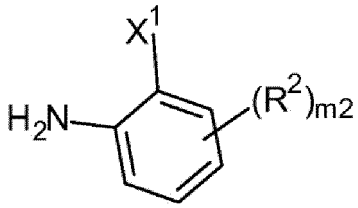
4. Procédé selon l'une quelconque des revendications 1 à 3, où le solvant est choisi parmi le diméthoxyméthane, le diéthoxyéthane, le 1,3-dioxane, le 1,4-dioxane, la N-méthylpyrrolidinone, le N,N-diméthylacétamide, le diméthylformamide et des mélanges de ces solvants.

5. Procédé selon l'une quelconque des revendications 1 à 4, comprenant la réaction d'un composé de formule



(**III**)

avec un composé de formule



(**IV**)

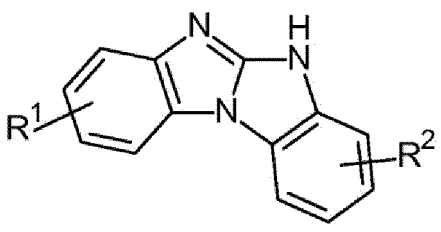
en présence d'un acide dans un solvant à température élevée pour obtenir un composé de formule (**II**), où

X^2 est Cl, Br ou I, en particulier Cl, et
m1, m2, R^1, R^2, et X^1 sont définis dans la revendication 1.

6. Procédé selon la revendication 5, où l'acide est sélectionné parmi l'acide méthane sulfonique, l'acide camphre sulfonique, l'acide p-toluène sulfonique, l'acide chlorhydrique et l'acide sulfurique.

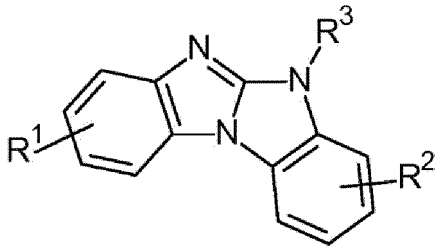
7. Procédé selon la revendication 5 ou 6, où le solvant est sélectionné parmi le diméthoxyméthane, le diéthoxyéthane, le 1,3-dioxane, le 1,4-dioxane, la N-méthylpyrrolidinone, le N,N-diméthylacétamide, le diméthylformamide et des mélanges de ces solvants.

8. Procédé selon l'une quelconque des revendications 1 à 7, lequel comprend en outre la réaction c1) de



(**Ia**),

avec un composé de formule R^3-X^3 (**V**), pour obtenir un composé de formule

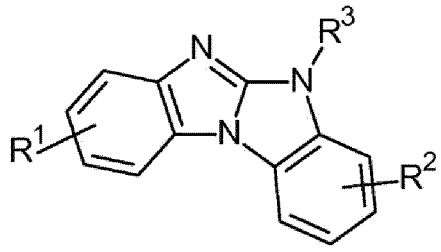


(**VI**),

où

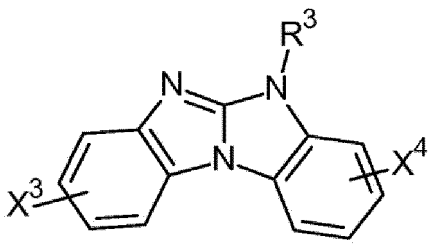
X^3 est Cl, Br ou I,
R^3 est un groupe aryle en C_6-C_{24} ou un groupe hétéroaryle en C_2-C_{30} ; et
R^1 et R^2 sont définis dans la revendication 1.

9. Composé selon la revendication 8, où le composé de formule



(**VI**),

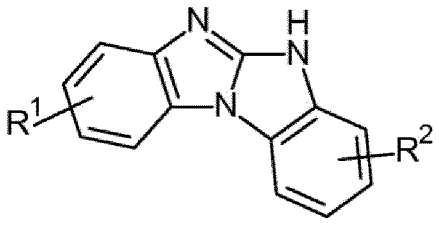
où R^1 et R^2 sont H, est halogéné pour obtenir un composé de formule



(**VII**),

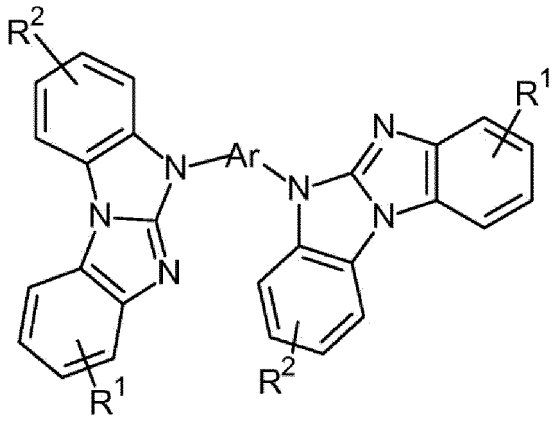
où
X^3 est Br ou I et X^4 est Br ou I et R^3 est défini dans la revendication 8.

10. Procédé selon l'une quelconque des revendications 1 à 7, lequel comprend en outre la réaction c2) de



(**I**),

avec un composé de formule X^5-Ar-X^6 (IX), pour obtenir un composé de formule

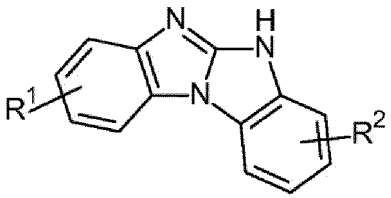


(**X**),

où X^5 et X^6 sont, indépendamment l'un de l'autre, Cl, Br ou I, Ar est un groupe de liaison divalent (hétéro)aromatique et R^1 et R^2 sont définis dans la revendication 1.

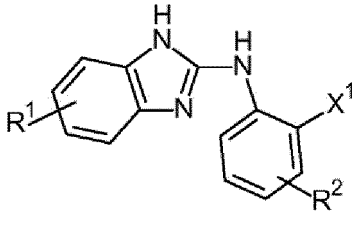
11. Procédé selon l'une quelconque des revendications 1 à 8, où m1 et m2 sont 0.

12. Procédé selon l'une quelconque des revendications 1 à 8, où le composé de formule (**I**) est un composé de formule



(**Ia**)

et le composé de formule (**II**) est un composé de formule



(**IIa**),

où

X^1 est Cl, Br ou I,

R^1 est alkyle en C_1-C_8, alcoxy en C_1-C_8, Br, Cl ou F, et
R^2 est alkyle en C_1-C_8, alcoxy en C_1-C_8, Br, Cl ou F.

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Patent documents cited in the description

- WO 2012130709 A **[0007] [0009] [0062]**
- WO 2011160757 A **[0009] [0062]**
- WO 2013068376 A **[0009] [0062]**
- WO 2014009317 A **[0009] [0062] [0070]**
- WO 2014044722 A **[0009] [0062]**
- WO 2015014791 A **[0009] [0062]**
- US 20020151456 A **[0066]**

Non-patent literature cited in the description

- **KHAN, MISBAHUL AIN ; RIBEIRO, VERA LUCIA TEIXEIRA.** *Pakistan Journal of Scientific and Industrial Research,* 2000, vol. 43, 168-170 **[0002]**
- **PEDRO MOLINA et al.** *Tetrahedron,* 1994, 10029-10036 **[0003]**
- **ACHOUR, REDDOUANE ; ZNIBER, RACHID.** *Bulletin des Societes Chimiques Belges,* 1987, vol. 96, 787-92 **[0003] [0007]**
- **HUBERT, ANDRE J. ; REIMLINGER, HANS.** *Chemische Berichte,* 1970, vol. 103, 2828-35 **[0004]**
- **X. WANG et al.** *Org. Lett,* 2012, vol. 14, 452-455 **[0005]**
- *Eur. J. Org. Chem.,* 2014, 5986-5997 **[0006]**
- **GUODONG YUAN et al.** *RSC Adv.,* 2014, vol. 4, 21904 **[0008]**
- **I.V. KOLESNIKOVA et al.** *Journal of Fluorine Chemistry,* 1988, vol. 40, 217-246 **[0009]**
- *J. Mater. Chem.,* 2008, vol. 18, 1296-1301 **[0064]**
- *Helvetica Chimica Acta,* 2006, vol. 89, 1123 **[0065]**
- *SYNLETT,* 2006, vol. 17, 2841-2845 **[0065]**
- *Synlett,* 2005, vol. 18, 2837-2842 **[0066]**
- *Synthesis,* 2005, vol. 10, 1619-1624 **[0066]**
- *Organic Letters,* 2010, vol. 12, 2194-2197 **[0066]**
- *Synlett,* 2006, 2841-2845 **[0066]**
- *Organic Process Research & Development,* 2006, vol. 10, 822-828 **[0066]**
- *Synthetic Communications,* 2007, vol. 37, 1381-1388 **[0066]**
- *Can. J. Chem.,* 1989, vol. 67, 2062 **[0066]**
- *Synthesis,* 2001, vol. 12, 1794-1799 **[0066]**
- *J. Heterocyclic Chem.,* 2002, vol. 39, 933 **[0066]**
- *Org. Lett.,* 2007, vol. 9, 797 **[0066]**
- *Macromolecules,* 2011, vol. 44, 1405-1413 **[0066]**
- *J. Heterocyclic Chem.,* 2001, vol. 38, 77 **[0066]**
- *J. Org. Chem.,* 2010, vol. 75, 2578-2588 **[0066]**
- *Synthesis,* 2008, 221-224 **[0066]**
- *J. Org. Chem.,* 2009, vol. 74, 3341-3349 **[0066]**
- *J. Org. Chem.,* 2006, vol. 71, 7422-7432 **[0066]**
- *Eur. J. Org. Chem.,* 2008, 1065-1071 **[0066]**
- *Chem. Asian J.,* 2010, vol. 5, 2162-2167 **[0066]**
- *Synthetic. Commun.,* 1998, vol. 28, 3225 **[0066]**